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Perceptual Learning of Lateral Interactions in the near-periphery of the visual field: New Perspectives for patients with Macular Degeneration

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Introduction

The aim of this thesis was threefold: solving an apparent controversy concerning the lack of consistency on peripheral, collinear facilitation, overcoming the apparent absence of perceptual learning modulation for lateral interactions in the periphery of the visual field and lay the foundations for developing a functional treatment for people with central vision loss (maculopathy patients).

Regarding the first point, in the realm of vision sciences, psychophysical studies over the last two decades challenged the rigid, hyerarchical structure usually proposed for describing the path of the visual information through the brain: while most of the models used for describing the visual analysis process assume that the visual information undergoes to a series of progressively higher computation, with the first stages analyzing simple feature and being local and independent, evidence from early 90s experiments showed forms of contextual modulation even at these first stages.

Electrophysiological and psychophysical studies showed how the response of a unit to a stimulus located within its receptive field could be modulated by stimuli placed outside the receptive field, sharing some basic feature such as orientation, spatial position and dimension. This high specificity suggests the involvement of early visual areas, such as visual area V1, in which units responding to similar stimuli (having the same orientation and spatial frequency sensitivity) interact.

Contrast thresholds modulations have been reported for different distances between the central stimulus and the so-called flankers stimuli.

In the specific, for short distances, up to 3 times the size of the target stimulus, these modulations are inhibitory, meaning that they produce and increase in contrast thresholds. Inhibitory effects are commonly considered effects from within the receptive field (same hypercolumn), so the presence of a flanker near the borders of the receptive

field produces an inhibitory response. Facilitatory effects are considered product of excitatatory connections between distinct but adjacent units.

These mechanisms seem to be the basis for the figure-ground segmentation and processing of image integration. Recently, similar effects have been studied in the periphery, but the lack of consistency brought researchers to question the similarities between fovea and periphery. In Experiment 1, we measured lateral interaction curves in normal-sighted subjects, showed that collinear facilitation is present in the periphery of the visual field, at a target-to-flankers distance larger than in fovea. Moreover, we showed the possibility of modulating this interactions through perceptual learning (in the specific, reducing the shorter-distances inhibition) and to transfer the learning to untrained, higher-level visual functions such as crowding reduction. In Experiment 2, we verified that the perceptual learning is specific for spatial position and local and global orientation of the training stimuli, suggesting an involvement of the early visual areas.

In the second section, we reported two experiments (Experiment 3 and Experiment 4) in which we applied the paradigm of perceptual learning on peripheral lateral interactions with people affected by maculopathy. This type of visual impairment produces the loss of central vision, and forces maculopathy patients to use a retinal location in periphery of the visual field as a new fixation point (PRL, preferential retinal locus).

In Experiment 3, tailoring the training on the characteristics of each patient, we showed the effectiveness of training both in improving the performance in the trained task but most importantly, in transferring to higher-level visual functions, in the specific Visual Acuity, both in the PRL and in a symmetrical retinal locus. Moreover, training seemed to produce improvement in the untrained eye as well. However, training did not produce crowding reduction, probably for a "roof effect" due to the natural, everyday training of these people.

In Experiment 4, we tried to overcome to a methodological problem that arose with the paradigm used in Experiment 3: changing the procedure, we were able to measure

peripheral lateral interactions in maculopathy subjects and to show the possibility of modulations for these interactions. Lateral interactions curves for the maculopathy subject tested showed, for the PRL, that collinear facilitation is already present at shorter target-to-flankers distances respect to normal subjects, while in the No-PRL, there seems not to be any collinear facilitation, even for the larger distances tested.

Taken together, the results of these studies indicate both the existence of collinear facilitation in the near-periphery of the visual field in normal-sighted and maculopathy subjects, and the effective possibility of developing a proper training, based on a simple and non-invasive technique, for enhancing peripheral visual functions in patients affected by central vision loss, improving the quality of their vision and, in turn, the quality of their lives.

Chapter 1

Center-surround and lateral interactions in the early visual cortex: an overview

The most common functional models of visual information processing suggest that in the early stages, the retinal image is analyzed independently by mechanisms that respond locally to a selected range of orientations and spatial frequencies. It is assumed that visual neurons have the so-called classical receptive field (CRF), that is the visual space whereby the presentation of a stimulus leads to action potentials. The cells of the early visual cortex (area V1) present a CRF that is restrict and orientation-selective..Theoretical assumptions state that stimuli located in the CRF's surround cannot activate the given unit. In recent years, , new techniques and renewed interest in this topic has led to increasing evidence that challenge the concept of CRF, pointing out that it is not the best model for defining the region that can influence the unit's response. A number of studies have indicated how stimuli located outside the CRF of a neuron can influence the response of the given neuron to stimuli located within its CRF, in an interaction called "center-surround" ((Kapadia, Ito, Gilbert, and Westheimer, 1995; Fitzpatrick, 2000; Fregnac and Bringuier, 1994). In this chapter, recent evidence regarding contextual phenomenon and surround modulations in the early visual cortex will be discussed, then psychophysical studies regarding lateral interaction at the fovea will be analyzed; finally research that has been carried out on lateral interactions in the periphery of the visual field will be described.

1.1 Center-Surround interactions

Electrophysiological studies helped opening the way to the most recent theoretical and experimental investigations in the center-surround interactions. Studies on animals, such as the ones carried on by Hubel and Wiesel (1958; 1963) ,showed how units present in the visual areas of cats (area 17, 18 and 19) and monkeys (area V1) were selective for some of the stimuli feature, such as length and width. These cells, defined as "hypercomplex", presented a response that was maximal for a given length, but then, increasing the dimension of the stimulus, started reducing to the point of suppression. These evidence suggested the existence of inhibitory zones surround the central area, located along the axis for which the unit is selective and on the flanks. These areas are usually defined as "end zones" and "side-bands", respectively and their discovery contributed to the idea of receptive field with modulation produced by its surround. More recently, rigorously investigating these modulatory effects with different stimuli placed in the center and in the CRF's surround, a number of studies reported evidence for center-surround modulation in most of the units that constitute V1. The modulatory effects of the surround most commonly produce inhibition of the unit's response:. Cell recording showed that up to 86% of units in cat's V1 area (Sengpiel, Sen, Blakemore, 1997) and more than 90% of neurons in monkey's V1 area (Jones, Grieve, Wang and Sillito, 2001) manifest suppression when the width of a stimulus located in their CRF is extended beyond its boundaries Some authors (Li and Li, 1994; Maffei and Fiorentini,1976) proposed that the area to which the unit is sensitive, comprising both its CRF and the surrounding region capable of producing modulation, is 2-5 times the dimension of the CRF itself. Some variability has been reported for the dimension of the surround and the area that can produce the strongest modulation, that could be asymmetric respect to the CRF's center. (Baudot et al., 2000; Freeman, Ohzawa and, 2001; Jones et al., 2001; Walker, Ohzawa and Freeman, 1999). The surround of the receptive field seems to show similar selectivity respect to the center, only broader (DeAngelis, Freeman, and Ohzawa, 1994; Li and Li, 1994): consequently, modulations

are usually stronger for surrounding stimuli with the same orientation (De Angelis et al., 1994; Knierim and Van Essen, 1992; Li and Li, 1994; Levitt and Lund, 1997; Sengpiel, et al., 1997; Sillito, Grieve, Jones, Cudeiro, and Davis, 1995; Walker et al., 1999) and spatial frequency (DeAngelis et al., 1994; Li and Li, 1994; Walker et al., 1999) as the central stimulus, reducing progressively for relative changes in these features between center and surround stimuli. Interestingly, these modulations seem independent from the stimulus' phase (Levitt et al, 1997; DeAngelis et al., 1994). This high selectivity leads to hypothize a cortical origin for these effects. Although most of the investigation on lateral interactions in V1 showed inhibitory modulation, a number of studies also showed the presence of facilitatory interactions. For stimuli located in the CRF, the relation between the target's contrast and the unit's contrast threshold seems to govern the direction of the modulation (inhibitory or facilitatory;.Mizobe, Polat, Pettet, and Kasamatsu, 2001; Polat, Mizobe, Pettet, Kasamatsu, and Norcia, 1998; Sengpiel et al, 1997). For example, a stimulus located in the surround of the CRF can produce inhibitory modulation for a high-contrast center stimulus and facilitation when the contrast of the central stimulus is reduced to that unit's threshold. The selectivity of facilitatory interactions is similar to that of inhibitory, with strongest modulation for center and surround stimuli having the same orientation and are located on the same axis.

1.1.1 Neural substrates

Despite the controversies related to the extent of excitatory regions outside the receptive field, it is quite clear that V1 units are influenced by stimuli located outside their CRFs. The extent of these connections makes it unlikely that they are due to divergent thalamo-cortical inputs and thus cannot be described as feedforward connections. The estimations of the thalamo-cortical axons would constitute a physical limit to the width

of this connection to a maximum of 2 mm. The influence of orientation and direction to the center-surround modulations and the presence of the effects also in case of dichoptic presentations contribute to the hypothesis of a cortical origin for these phenomena. Therefore, most of the proposed models of early visual computation assume the existence of a network of horizontal connections in V1, localized in layers 2/3. These connections come from pyramidal cells and can reach a length of several millimeters (Gilbert and Wiesel, 1983; Kisvarday, Toth, Rausch and Eysel, 1997; Martin and Whitteridge, 1984; Angelucci, Levitt and Lund, 2002; Sincish and Blasdel, 2001). The hypothesis that these type of projections are responsible for long-range interactions are supported by the evidence of orientation and location selectivity of center-surround modulations. This is likely because pyramid cells tend to connect units with similar orientation selectivity, specifically, cells whose receptive fields are topographically aligned along an axis of collinearity for distances over 700 μm (Schmidt, Goebel, Lowel, and Singer, 1997; Bosking, Zhang, Schofield, and Fitzpatrick, 1997; Chisum, Mooser, and Fitzpatrick, 2003; Sincish et al, 2001). Moreover, these cells interact with both inhibitory and excitatory units, so they could be responsible for both long-range monosynaptic excitation and long-range disynaptic suppression (McGuire, Gilbert, Rivlin, and Wiesel, 1991; Tucker, and Katz, 2003; Tucker and Katz, 2003). On the other hand, hypoteses involving feedback connections from higher-level, extra-striate areas (such as V2, V4 or MT) are not excluded. It is already known that the activity of V1 could be modulated by feedback connections controlling the response gain of their target neurons (Shao and Burkhalter, 1996). Evidence shows how the inhibition of V2 or MT produces a decrease of V1 responses (Mignard and Malpeli, 1991). Furthermore, units in these higher-level areas are characterized by larger receptive fields respect to V1 units, so they can analyze a wider area of the visual field (studies on monkeys showed that projections from V2 to V1 can gather information from an area 5-6 times larger than the one of V1 units) (Angelucci, Levitt,Walton, Hupé, Bullier, and Lund, 2002). Like horizontal projections, feedback connections are characterized by

dishomogeneous distribution. There are studies supporting the hypothesis that they connect areas of like-orientation preference (Angelucci et al., 2002; Gilbert and Wiesel, 1989; but see Stettler, Das, Bennett, and Gilbert, 2002, for a different result) and in the macaque, cover anisotropic parts of the visual region (Angelucci et al., 2002). While it seems that feedback connections play a role in shaping the activation of V1 units, other evidence puts into question the importance of these interactions, supporting the role of horizontal connections. Firstly, inhibition of area V2 does not influence the response modulation by static texture surround in V1 units (Hupé, James, Girard, and Bullier, 2001). Secondly, the horizontal connections seem denser than the feedback projections (Stettler et al., 2002). Moreover, these two types of connections differ in the temporal dynamics; in studies using single cell recording from visual cortex during subthreshold processing of lateral input, horizontal connections exhibited slow conduction dynamics (Bringuier, Chavane, Glaeser, and Fregnac, 1999; Chavane, Bringuier, Baudot, Monier, Borg- Graham, Lorenceau, and Fregnac, 2000). On the other hand, feedback connections seem very fast, showing a response within few milliseconds with respect to the V1 responses (Hupé, James, Girard, Lomber, Payne, and Bullier, 2001). This evidence seems consistent with the dynamics of the lateral diffusion of subliminar activity elicited by the activation of the surround (Bringuier et al., 1999; Grinvald, Lieke, Frostig, and Hildesheim, 1994; Rossi, Desimone, and Ungerleider, 2001). Hypothesis based upon these findings propose that both connections contribute in center-surround modulation. Horizontal connections mediate the near interactions, such as those located within the summation field, while feedback connections modulate responses connecting the distant surround (Angelucci et al., 2002; Brown, Allison, Samonds, and Bonds, 2003; Cavanaugh et al., 2002; Chisum et al., 2003).

1.1.2 Models for center/surround modulation

The idea behind the function and the structure of V1 has dramatically changed after the evidence that interactions take place between units at the early levels of visual processing. Centre-surround modulations revealed that these units interact in a non-linear way, making a model of visual processing that only takes into account the computation of individual units' activity insufficient.

A theory of early visual processing that integrates the information that V1 units interact with horizontal connections should be able to account for different questions:

-what type of transformation is performed by single V1 units during the presentation of a display with a central stimulus and a surround?

-what is the connection between this non-linear computation and the features of V1 units?

-What role do center-surround modulations play in shaping visual perception?

Three models have been proposed to account for these questions:

1. *functional models*, which aim at finding the response properties within the context of a visual information processing algorithm;
2. *structural models*, focus on finding the neural structures and mechanisms involved in the modulation processes;
3. *optimized models*, aim at predicting the physiological data on the basis of strategies of visual coding.

1.1.3 Functional models

Studies on functional models started with surround suppression experiments: authors attempted to propose a model defining the properties of the so-called extended receptive field ERF, which was intended as the unit of classical receptive field and its proximal surround (Cavanaugh, et al., 2002; Sceniak, Hawken, and Shapley, 2001; Sceniak et al., 1999). Sceniak et al. (2001; 1999) proposed a model in which the ERF is constituted by 2 overlapping, subtracting mechanisms defined by a difference of Gaussins (DoG). These two gaussians respectively represent the excitatory activation of the central CRF (assumed to correspond to the envelope of a Gabor function representing the CRF's spatial structure) (Jones and Palmer, 1987), and the surround's suppressive contribution However, this model assumes a linear interaction between surround and center mechanisms, while various experimental evidence supports a non-linear integration (Polat, 1993, 1994a; Cavanaugh et al., 2002). It seems that the surround's influence on the unit's contrast response can be better defined by a vertical scaling of the curve in log-linear coordinates (a change in response gain, corresponding to a divisive mechanism) rather than a downward shift and thresholding of the curve, which would correspond to a subtractive mechanism.

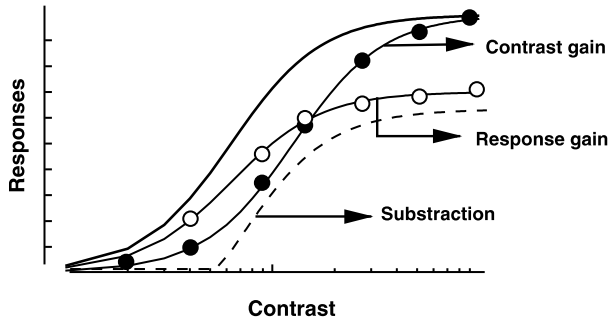

Figure 1: (from Seriès et al., 2003)

Hypothesis for suppressive effects of the surround. The bold curve represents the response of a unit to a stimulus located in its CRF as a function of contrast in log-linear coordinates.

1- Contrast gain: the suppressive effect could produce a horizontal shift in V1's units contrast response curve. This does not change the maximal response of the units but scales their contrast sensitivity

2- Response gain: suppressive effects could compress the curve ordinates. This does not change the range of contrasts at which the unit responds but only scales activities for all the contrast by a constant ratio.

3- Subtraction: surround stimuli can produce a reduction in responses by the same amount for all the contrast.

Changes in both contrast gain and response gain are divisive forms of suppression.

Effects of suppression within the CRF seem to fit better with a contrast gain model (Carandini, Heeger, and Movshon, 1997; Sengpiel, Baddeley, Freeman, Harrad, and Blakemore, 1998), while a response gain model fits better for surround suppression.

Cavanaugh et al. (2002) suggested a different model based on the ratio of Gaussians . This model can be considered as an upgrade of the standard normalization model (Albright and Stoner, 2002; Heeger, 1992) since it accounts for the surround effect (Chen et al., 2001; Schwartz and Simoncelli, 2001; psychophysical evidence: Olzak and Laurinen, 1999; Snowden and Hammett, 1998; Xing and Heeger, 2001). The standard normalization model proposes that the activity of each unit is normalized by the responses of a pool of surrounding units, chosen uniformly in a local neighborhood (i.e.

within the same hypercolumn). These effects are supposed to be non-specific, or broadly selective for orientation and spatial frequency.

This model is in line with the nonlinearities reported in those responses to stimuli located within the CRF (Albright et al., 2002; Heeger, 1992). The RoG model elaborates this description by proposing that units responding to surround stimuli can also contribute to the "normalization pool". However, since surround suppression is selective to the central stimulus' features, the units contributing to surround normalization pool cannot be chosen uniformly but specifically within the areas in which the preferences for orientations and spatial frequencies similar to that of the CRF (Schwartz et al., 2001). DoG and RoG models are quite popular because they can fit experimental data, such as summation curves. Moreover, they are consistent with the reported expansion of the size of the RF when contrast decreases (Sceniak et al., 1999, Cavanaugh, et al., 2002; Chen et al., 2001,) change dynamically for contrast variations. These phenomenological models provide a simple characterization of the main features of surround modulations, that can be used in large-scale analysis of visual processing, helping to understand their functional consequences. On the other hand, these models do not define any neural mechanism of circuits involved in these functions, reducing in turn their predictive power for physiological data.

1.1.4 Structural models

There have been attempts to create a unitary model that can account for the different behaviour of the neural network depending on the stimuli configuration:

Stemmler et al. (1995) and Somers et al. (1998) aimed to understand how surround facilitation for a central target with low contrast and surround suppression for high contrast can be explained by a single network with fixed connections.

These models describe some of the hypercolumns present in V1 as constituted by excitatory and inhibitory units. For each hypercolumn, there are circuits responsible for the properties of the CRF and the local balance between excitation and inhibition. At the single-unit integrative level, both models assume asymmetrical functional threshold and response gain between excitatory and inhibitory units: for weak stimuli, inhibitory units are not activated, while for strong stimuli, the inhibitory neurons are rapidly activated, causing the response saturation of the excitatory cells. This asymmetry could depend on the spiking features of excitatory and inhibitory units (McCormick, Connors, Lighthall, and Prince, 1985). Another hypothesis is that it could be the product of differences in the efficacy or kinetics of activity-dependent depression between intracortical excitatory, thalamo-cortical exicatory and inhibitory synapses (Somers et al., 1998; Thomson and Deuchars, 1997) or different levels of spontaneous activities for excitatory and inhibitory units (Stemmler, et al., 1995). In both models, authors proposed that the different hypercolumns interact via long-range horizontal excitatory projections, connecting units with similar orientation preference and producing synapses on both excitatory and inhibitory neurons. Consequently, the effect of the surround could be defined as an orientation-specific modulation of the local excitation/inhibition balance. The activity of these models can be defined by simple firing-rate models of a cortical column (Ernst, Pawelzik, Wolf, and Geisel, 1999) or hypercolumn (Stetter, Bartsh, and Obermayer, 2000), constitued of excitatory and inhibitory units, both receiving inputs in response to a central stimulus, plus additional excitatory inputs when the surround is activated.

These models are based on a simple mechanism:

-when the center stimulus' contrast is low, the local inhibitory units are inactive. The excitatory input from the surround is lower than their activation thresholds. However, they amplify the responses of the excitatory units.

-increasing the center stimulus' contrast leads in turn to activation of the inhibitory cells. Therefore, the surround enhances the activity of the inhibitory units, provoking a reduction in the response of excitatory cells.

Both models provide explanation for the reported expansions of the size of V1 receptive fields (SSF) when contrast decreases (Kapadia et al., 1999, Sceniak et al., 1999). Expanding a central stimulus beyond the MDF produces a recruitment of horizontal connections. In low contrast conditions there is a progressive enhancement of the response, on the other hand, with high contrast conditions, the spatial expansion of the stimulus beyond the MRF produces a suppression of the response.

The mechanisms described by these models support the idea that the contrast dependency of the size of the receptive field is directly related to the contrast sensitivity of the center-surround interactions. Moreover, it fits with evidence from intracellular recordings that length-tuning is absent for low contrast stimuli (Anderson, Lampl, Gillespie, and Ferster, 2001).

Other authors, like Dragoi and Sur (2000) proposed a different model, aiming to account for another phenomena regarding center/surround modulation that previous models were not able to address: V1 units can be facilitated beyond optimal levels when the surround stimuli are cross-oriented respect to the central stimulus, while they are suppressed when the surround is iso-oriented (Levitt and Lund, 1997; Sillito et al., 1995). At the local level, the model broadly describes tuned inhibitory cells of different orientation preference that interact. At long-range level, surround effects are mediated by excitatory horizontal connections, that link preferentially units of similar orientation. Suppression in the iso-oriented condition as previously explained, is the product of excitation of the local inhibitory neurons with same orientation selectivity as the recorded unit. Cross-oriented facilitation is explained as disinhibition of these local interneurons, through the activation of another pool of inhibitory units, specific for the same orientation as the surround stimulus (Fregnac and 1996). One of the main predictions of these models is that the nature and selectivity of long range connections

between hypercolumns crucially depend on the characteristic of the local circuits within the hyperolumn and excitatorty/inhibitory balance of the aforementioned neurons, which change with orientation and contrast. As a consequence, it is not always easy to distinguish between surround modulation and local properties of the CRF. Issues regarding the orientation selectivity (Ferster and Miller, 2000 and contrast gain control mechanisms (Abbott, Sen, Varela, and Nelson, 1997; Somers et al., 1998) make it difficult to develop a more comprehensive model of center-surround modulation. It is interesting to note that most of the proposed models do not take into account the functional diversity present at the single cell level, assuming cortical homogeneity of structure and function. However, clear heterogeneities of local circuits have been observed in recent studies, depending on the position in the orientation map (Schummers, Marino, and Sur, 2002) or in the different cortical layers (Martinez, Alonso, Reid, and Hirsch, 2002). It seems plausible to suggest that this heterogeneity is reflected in the form of lateral modulations. Moreover, the models of Somers et al. (1998), Stemmler et al. (1995) and Dragoi and Sur (2000) are theoretically compatible (Seriès, 2002). However, the latter requires that strong connections exist between (inhibitory) cells of orthogonal orientation. The presence of these cross-oriented, inhibitory interactions is still debated (Ferster and Mille, 2000). Recently, electrophysiological studies seem to have localized these connections to the synaptic level (Monier, Chavane, Beaudot, Graham and Fregnac, 2002). A possibility is that the different local networks present in the orientation map produce different types of lateral modulations. (Das and Gilbert, 1999, Seriès, 2002). Anatomical evidence from cat's area 17 showed that units with similar suppressive or facilitatory surround have the tendency to organize in spatial clusters (Yao and Li, 2002), and this is in agreement with this hypoyhesis.

1.1.5 Optimized models

Recent attempts to describe functional and structural models of center/surround modulations have contributed to further investigate these phenomena in terms of their main features and underlying circuits. An open question is related to the functional role of these connections. Recent studies suggested the possibility that they are involved in the optimization of the coding of visual inputs (Rao and Ballard, 1999; Simoncelli and Schwartz, 1999; Vinje and Gallant, 2000). One of the theories regarding the role of these connections suggest that sensory units modify their integrative properties in response to the statistical characteristics of the input signals, in order to remove noise in the sensory information and as a result, producing different and statistically independent neural responses (Attneave, 1954; Barlow, 1961). Models of early visual analysis based on this hypothesis have been created using different criterion of statistical optimization and verifying whether the output is similar to the response of a set of neurons (Simoncelli and Olshausen, 2001). This approach lead to the creation of some models that have been proven to be successfull in accounting for the structure of V1 receptive field (Bell and Sejnowski, 1997; Olshausen and Field, 1996). On the other hand, since they are constrained by linear operations, they are not able to produce completely independent responses (Schwartz and Simoncelli, 2001; Simoncelli and Schwartz, 1999). However, Simoncelli and Schwartz (1999, 2001) showed that the residual dependency could be eliminated by using a different version of the aforementioned RoG model, i.e. a non-linear form of analysis that rectifies and normalizes the linear response of each function by a weighted sum of the responses of neighboring units. In the case of maximization of response independence, as result of weights change, the model predicts some suppressive effect, similar to the main properties of surround suppression (e.g. the selectivity for orientation, spatial frequency and distance between center and surround stimuli). Rao and Ballard (1999) suggested the idea of "predictive coding" in accounting for surround effects: neural circuits learn

statistical regularities from the world, and then they report deviations from these regularities. All the information which is not different from the regularities are consequently inhibited. In their model, each stage of the hierarchically organized visual analysis attempts to predict the responses at the next, lower level through feedback connections. The difference between the prediction and the real response is sent via feedforward connections and used to estimate the input signal at that stage. In this framework, Rao and Ballard (1999) interpreted center-surround interactions as the detection of residual difference, reporting discrepancies between input signal and its statistical prediction on the basis of an internal model of natural world.

2. Center-surround modulations and psychophysical lateral interactions

Visual perception does not strictly resemble the physical characteristics of the natural scenes. It is more a product of complex mechanisms that help in interpreting visual information. Contextual effects contribute to perceive the world as a global and structured ensemble, instead of a series of isolated elements, and features of single elements, such as orientation, spatial frequency and contrast, are interpreted according to the context (Wertheimer, 1923). This perceptual organization, reported by Gestalt psychologists in the early ‘900, has not always been easily integrated with the studies of brain’s visual analysis. However, recent years saw a renewed interest in a psychophysical approach to the study perceptual organization. A number of studies showed how the mechanisms responsible for perceptual organization are not located in higher-level visual areas, but are a product of early visual areas, such as V1. Furthermore, these studies showed similarities between how the presence of a stimulus

can modulate the perception of another, as psychophysically demonstrated, and center-surround modulations, observed electrophysiologically.

Polat and Sagi (1993) used a threshold detection task with lateral masking displays in order to investigate spatial interactions between visual channels selective for spatial locations. Presenting foveally a Gabor target, flanked by two Gabor patches located at the same lateral distance respect to the target, authors measured contrast thresholds for different target-to-flankers distances. Respect to previous studies on lateral masking (Bouma, 1970; Flom, Weymouth and Kahneman, 1963b; Flom, Heath and Takahashi, 1963a), that used alphanumeric characters as testing stimuli, Polat and Sagi (1993) used a simpler type of stimuli, that are Gabor patches. Moreover, they adopted a different task: while aforementioned studies used letter recognition tasks, authors applied a two-alternative forced choice (2AFC) paradigm to a contrast detection task. The rationale behind this choice is the possibility of distinguishing between two different processes that can contribute to masking effect, namely integration processes that take place within filters (and that are assumed to be linear) and interactions between filters (where nonlinear processing take place). By using Gabor patches, that are localized band-pass stimuli, Polat and Sagi (1993) were able to control more precisely the set of channels involved in the detection of the stimulus, reducing the number of overall active neurons. Since the size of the filter is assumed to have a width twice its most sensitive wavelength (Watson, Barlow and Robson, 1983; Wilson, 1983), authors were supposed to find interaction from within the filters integration processes within this separation. The interpretation of results appears more complex when adopting low-pass stimuli as letters (Bouma, 1970), line elements (Kulikowski and King-Smith, 1973) or light spots (Westheimer, 1967).

These types of stimuli are low-pass and broad band in the spatial frequency domain and consequently, taking into account lateral interactions, elicit mostly within filter integration process through the activation of relatively large (lower frequency) filters that encompass both target and flankers. Previous studies adopting light spots' detection

on a background of a larger adapting field were discussed in terms of retinal inhibition (Westheimer, 1967), while results from line detection tasks with stimuli flanked by two masking lines were interpreted in terms of linear integration within spatial filters (Kulikowski and King-Smith, 1973). The configuration used by Polat and Sagi (1993), with Gabor stimuli placed in different spatial locations, allowed for a more precise investigation on the interactions between neighboring channels.

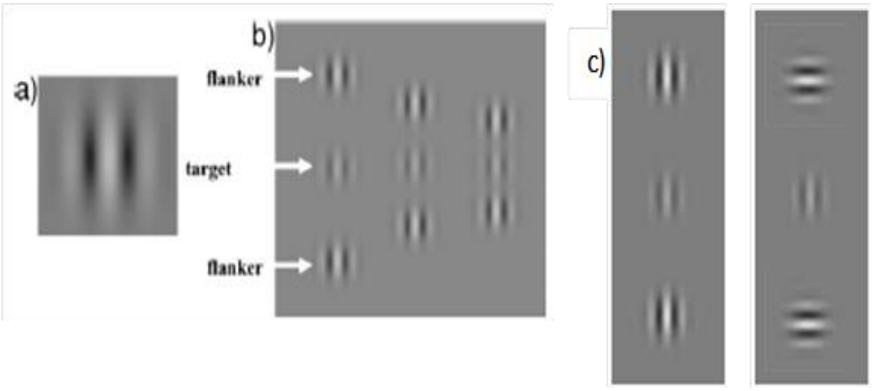

Figure 2*:* example of stimuli used by Polat and Sagi (1993) for the investigation of lateral interactions. a) a single Gabor patch; b) typical configuration with target and flankers, located at different separations.

The results of their study showed the existence of two regions in which contrast thresholds were modulated, one inhibitory and one excitatory, along the target-to-masks separations, indicated as λ (the wavelength of the Gabor stimulus).

In the inhibitory region, up to 1.5 λ of separation, contrast thresholds were higher, with a maximum elevation at the separation of one wavelength. Beyond 3 λ of separation, threshold decreased. This area of thresholds reduction is larger than the inhibitory one, starting at 1.5-2 λ, reaching a maximal elevation at 3 λ and then smoothly coming back to the normal threshold around 12 λ. Since the range is larger than the signal size

($\sigma = \lambda$), the increase effect cannot depend on overlapping between test and mask. Polat and Sagi (1993) also reported that the control experiment carried out to verify whether the effect was due to linear integration, showed that when using tests and masks of opposite phase the results did not differ. Moreover, for distinguishing between modulation of thresholds due to signal wavelength and modulation of threshold due to signal size, authors tested different σ / λ values. Results showed that the relevant parameter in thresholds' modulation is the wavelength (λ) and not the signal size (σ) or absolute space distances. Moreover, Polat and Sagi (1993) tested the specificity of the contrast threshold modulations for the orientation and spatial frequency of the flankers, while the target was kept constant. Modulation effects were still observed for target-flankers orientation difference of 15 deg but disappeared for 90 deg difference. They also noted that the facilitatory zone of the thresholds curve seemed more selective for orientation than the inhibitory zone. Regarding the influence of differences in target and masks spatial frequencies, Polat and Sagi (1993) reported that there is a narrower spatial frequency selectivity for the enhancement effect. The overall scheme of results reported by Polat and Sagi (1993) resembles in some ways the masking results from the spatial frequency domain. Tolhurst and Barfield (1978) studied inter-frequency masking effect with spatially extended, overlapping sine-wave gratings. They reported threshold suppression for similar frequencies between target and masks, while reporting an enhancement for the difference of two factors or more. The results or Polat and Sagi (1993) show a similar phenomenon in the domain of localized stimuli. Moreover, both effects seem to be similar in magnitude (0.4 log units) and also the enhancement zone is larger and more effective. Furthermore, Kulikowski and King-Smith (1973) studying contrast thresholds modulation for the detection of a fine line presented with two flanking sub-treshold lines, showed enhancement for small target-to-mask distances
(< 0.05 deg) and supression for target distances (up to 0.15, comparing to the 2 deg reported by Polat and Sagi (1993) as maximal distance for enhancement), probably probing within filter integration processes. This reversed effect could be due to the use

of sub-thresholds masks (Nachmias and Sansbury, 1974). Overall, the results of Polat and Sagi (1993) can be considered as the psychophysical demonstration of the existence of interaction of both excitatory and inhibitory in nature in the space domain, similarly to what Tolhurst and Barfield (1978) showed for the frequency domain. Tolhurst and Barfield (1978) suggested that channels are excited by frequencies up to one octave from their ideal frequency and inhibited by a broader range of frequencies. Consistently, Polat and Sagi (1993) proposed a similar pattern of connections for the space domain: channels could be excited by other channels within two wavelengths of distances and inhibited beyond that. These connections are not constrained to the same layer of filters, like in a feedback connection-network. Similarly, a feedforward network in which higher level units integrate the thresholded output of local band-limited filter should have a similar outcome, adopting an antagonistic weighting function. The parameters of this function, stated Polat and Sagi (1993), can be derived from their results, with a central, excitatory zone of two wavelengths as radius and beyond that an inhibitory area up to eight wavelengths of distance. This spatial distribution of excitatory and inhibitory areas is not much different from what Sagi (1990) proposed in a study on texture discrimination (3λ for inhibitory and 9λ for excitatory area). The 2 λ inhibitory zone is larger than the size of the spatial filters (Watson, Barlow and Robson, 1983; Wilson, 1983), while the excitatory region overlaps with filter size and could reflect at least in part spatial integration within the filter receptive field. Polat and Sagi (1993) pointed out that the correlation between neural inhibition and enhancement of sensitivity is not a paradox: direct inhibition on the target area could reduce spontaneous activity (and thus noise) near the area of detection, improving in turn the detection rate. Consequently, the enhancement after the inhibition may constitute a threshold effect that should reverse when the contrast judgment is produced on a suprathreshold target. The existence of such a suprathreshold effect has been reported in contrast judgment experiments (Chubb et al., 1989; Sagi and Hochstein, 1985). Cannon and Fullenkamp (1991a) using small sine-wave grating stimuli on high contrast surround gratings, reported the suppression

of the apparent contrast for the target grating. Authors stated that this suppression effect can be defined by a monotonic function, with suppression decreasing when the distance between target and surround increases. They reported a strong effect in an area up to five wavelengths from the target, progressively decreasing until ten wavelengths. Furthermore, in a second study, Cannon and Fullenkamp (1991b) also reported contrast enhancement, although only for some subjects. This effect seems consistent when the contrast of the stimulus is low and the surround width is small, compatible with a contrast dependent mechanism. Polat and Sagi (1993) argued an alternative explanation for their data on lateral interactions by hypnotizing a network with inhibitory connections between neighboring channels. On the basis of this assumption, threshold suppression is a result of direct inhibition, while threshold enhancement is a product of dishinibition. Consequently, their model assumes a certain amount of spontaneous activity, high enough to maintain inhibition between adjacent channels. The presence of a mask at some distance could produce inhibition for the channels near the target, reducing their inhibitory interactions and in turn facilitate target detection. But Polat and Sagi (1993) stated that this inhibitory model is somehow less plausible, since the two areas observed had different tuning for orientation and spatial frequencies. Overall, these data provided direct evidence for lateral interactions between spatial channels. Moreover, these interactions go beyond the area defined by linear integration within single receptive fields. The spatial parameters of these data are consistent with previous studies on human texture segmentation (Sagi 1990; Rubenstein and Sagi, 1990). Long range interactions between units codifying similar orientations have also been pointed out from recordings of the visual cortex (Gilbert and Wiesel, 1989; Grinvald, Ts'o, Frostig, Lieke, Arieli and Hildesheim, 1989) and are likely to be the underlying mechanism for the psychophysical effects reported by Polat and Sagi (1993).

In 1994, Polat and Sagi investigated the architecture of lateral interactions by varying global configuration of the target and masking stimuli, so the three Gabors were presented parallelly, orthogonally or diagonally respect to the global orientation

produced by the triplet.

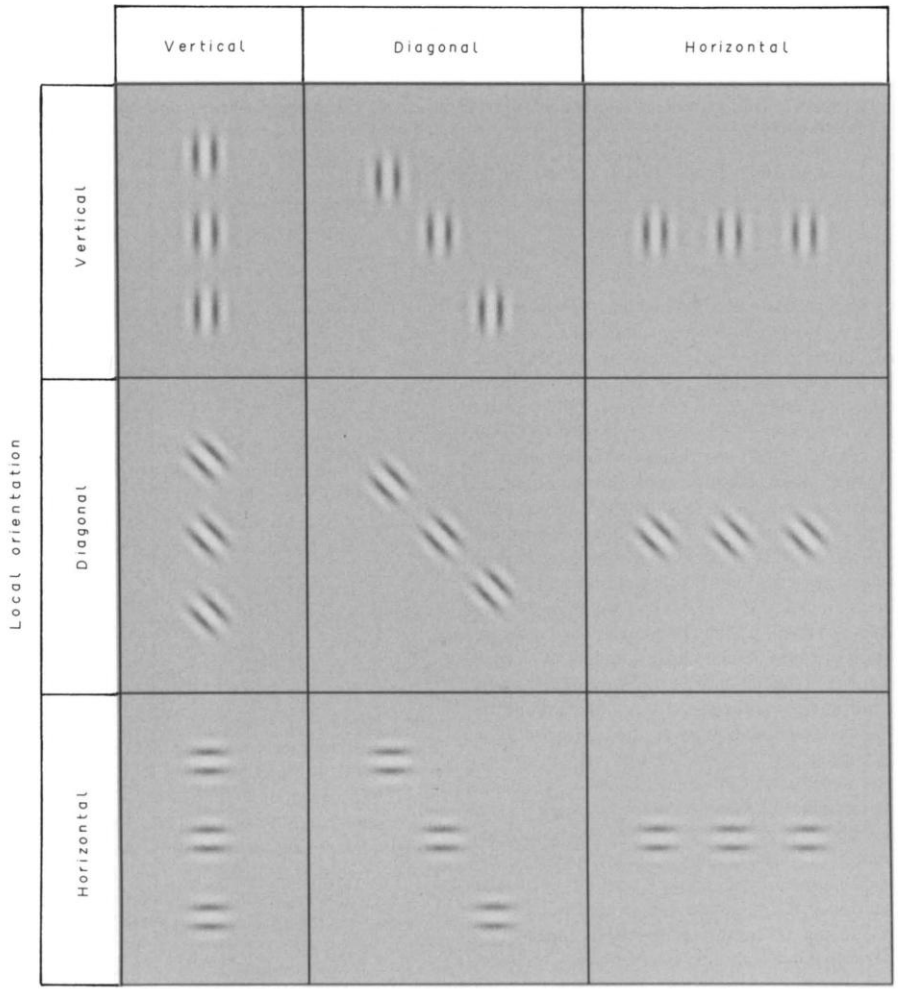

FIGURE 1. The configurations and orientations, both global (θ_g) and local (θ_l) of the stimuli used. (For diagonal θ_g we used also $\theta_l = 135$ deg, however, this configuration is not presented in this figure.) Only one target to mask distance is depicted here, but several were tested. See Methods for more details.

Figure 3: from Polat and Sagi (1993): configurations of the stimuli with global and local orientation varied throughout the experiment

Polat and Sagi (1994a) showed that magnitude and range of the thresholds' enhancement are a function of the offset between the orientation of the Gabor target and

the direction draw by the ideal line connecting the two flankers. An increase of 100% in the contrast sensitivity was observed for 0 offset, while for the 90 deg offset the increase was around 50%. Diagonal configurations lead to small variations. Target and masks orientations and locations did not influence sensitivity. Consequently, lateral interactions seem to be organized along a main direction aligned with the local orientation, with less influence for the orthogonal direction and no effect for diagonal directions. Studies on illusory contour through psychophysical measures showed an effect of threshold detection facilitation far from the edges of the inducing elements (Dresp, Free and Bonnet, 1992) but solely for the condition in which the two inducing elements are located along the same induction axis. This evidence is consistent with collinear and cooperative boundary completion (Dresp and Bonnet, 1991), studies of "collector units" (Morgan and Hotopf, 1989; Moulden and Zablocki, 1992), line integration (Field, Hayes and Hess, 1993) and Glass patterns (Sagi and Kovands, 1993). Field and colleagues (1993) reported that subjects were able to identify the path of Gabor stimuli presented on a background with randomly oriented elements, if the elements were oriented up to +/- 60 deg relative to one another (Field et al., 1993). Changing the surround elements' alignment to an orthogonal configuration led to a reduction of subjects' ability in identifying the stimulus. This report is consistent with the pattern of spatial interactions observed by Polat and Sagi (1994a), suggesting a mechanism for line segmentation. Moving a step forward, Field et al. (1993) suggested that their result for line integration could also lead to the hypothesis of a mechanism for detection curvatures. However, Polat and Sagi (1994a) reported that in experiments with flankers aligned along the curved line, there were no effects of enhancement, although they explained this lack of evidence by pointing out the different tasks used (detection of a single Gabor stimulus at threshold vs. following the path of 12 high-contrast Gabor stimuli). The structure of spatial interactions, as it emerges from Polat and Sagi (1994a) and hypothesized by Mitchison and Crick (1982) would play an important role in line segmentations, illusory contours and filling-in gaps. Moreover, these mechanisms could

be involved in object contour identification. Polat and Sagi (1994a) reported a significant interaction along the orthogonal direction respect to the contour, which they suggested as being of the same type as the main axis interaction, but probably with different underlying neural structures. Nelson and Frost (1985), in a study of single cell recordings from cat striate cortex, reported the presence of facilitatory lateral interactions along the cell's main axis and inhibitory ones in the other directions. Studies on orientation selective neurons in monkey's V1 showed that their responses can be reduced due to the presence of flanking lines with similar orientations, on either direction from the cell's position (Van Essen, DeYoe, Olavarria, Knierim, Fox, Sagi and Julesz, 1989). On the basis of this evidence, Polat and Sagi (1994a) interpret their effects as the product of strong neuronal facilitation (for the coaxial enhancement), disinhibition (the orthogonal enhancement) and inhibitory-excitatory balance (the lack of diagonal interactions).

2.1 Time course of lateral interactions

In 2006, Polat and Sagi investigated the temporal course of collinear lateral interactions, reporting an asymmetry: a classical modulation of lateral interactions was reported when flankers preceded the target, but not when the target preceded the flankers. This evidence, incompatible with feedforward models of lateral interaction, states that the two temporal effects are linearly summed within a higher level receptive field. Authors suggested that both facilitation and masking are the product of different time course for the two interactions, both excitatory and inhibitory.

Linear summation can account for simultaneous masking (Foley and Legge, 1981; Zenger and Sagi, 1996), but fails to explain the temporal asymmetry reported by Polat and Sagi (2006). Authors suggested that the two types of modulations, facilitation and inhibition, are the product of excitatory and inhibitory interactions within the neural

networks responding to visual stimuli (Adini et al., 1997; Hirsh and Gilbert, 991; Polat et al., 1998). Different temporal responses for excitation and inhibition modulations are consistent with the reported temporal asymmetry. Excitations appears to be slow in development, lagging behind the stimulus both in onset and offset, whereas inhibitions are faster and follow the onset and offset of the stimulus more closely. The presence of flankers activate both excitatory and inhibitory modulations in the processing stage, responding directly to the flankers and units that are triggered indirectly by lateral interactions, reaching a stable state whereby the two processes are in balance. This hypothesis is consistent with the slow time scale of lateral interactions (Bringuier, Chavane, Glaeser and Fregna, 1999; Grinvald, Lieke, Frostin and Hildesheim, 1994) and strong transient (Borg-Graham, Monier and Fregnac, 1998) and fast inhibition (Bair, Cavanaugh and Movshon, 2003). When the flankers precede the target, the presentation of the formers triggers both excitatory and inhibitory processes, with inhibition decaying when the flankers disappear. As a consequence, the unit's response to the target is summed at the slowly decaying excitatory effects promoted by the flankers (Tanaka and Sagi, 1998,1998b). When the flankers are presented simultaneously alongside the target, the low input produced by the target shift the response of the network towards excitation. When the target precede the flankers, the rapidly emerging inhibition produced by the flankers contrasts the sustained excitation. When the flankers are continuously presented on the other hand, both processes (inhibitory and excitatory) are activated, so there is no evident effect on the units responding to the target. This hypothesis is consistent with a previous account of masking, assuming transient inhibition contrasting persisting excitation (Breitmeye, 1984), but, differs from the account that assumes that both processes remain active as long as the stimulus is present. As stated earlier, neural models assume that facilitation by flankers presented at a separation of 3 λ or more from the target indicates effects from outside the CRF responding to the target's receptive field which is estimated as being around 2 λ (Mizobe et al., 2001; Polat, 1999; Polat et al, 1996; Polat and Sagi,

1993; Zenger and Sagi, 1996). Inhibitory modulations for target-to-flankers distances of 2 λ are considered as being integration within the RF, while separation of 3 λ or more reflects lateral interaction activations between different neurons responding to the target and the flankers. Lateral interactions are slow respect to the visual input that the RF receive, and that is because lateral interactions from outside the RF are transmitted through lateral connections. Tanaka and Sagi (1998b) reported a speed of about 3°/s for the transmission of lateral interactions, consistently with intracellular and optical imaging experiments (Bringuier et al, 1999; Grinvald et al., 1994). Physiological studies provide an estimation of the duration of the target response, indicating a limit of 200 ms (Albrecht, 1995; Mizobe et al., 2001; Polat et al., 1998). Similarly, psychophysical experiments indicate that integration for contrast is 160-200 ms at detection threshold (Watson, Barlow and Robson, 1983). Consequently, facilitatory effects can take place only if the transmission of the excitatory input from the flankers is not delayed by more than the duration of the feedforward input (<200 ms). For target-to-flankers separation of 3 λ, the estimated time of transmission is around 120 ms. Thus, in the case of simultaneous presentation of the flankers and target, the lateral transmission reaches the unit responding to the target in about 120 ms, that is within the persistence time of the target, thus producing facilitation. In the case of the presentation of flankers prior to the target, the response from the flankers was advanced by 60 ms (Polat and Sagi, 2006), so it reached the target location 60 ms earlier respect to the condition of simultaneous presentation of flankers and target. In the case of flankers presentation after the target, the response coming from the flankers is delayed by 60 ms, reaching the target location after 180 ms (near the observed limit for the integration and consequently failing to produce facilitation).

2.2 Perceptual learning and lateral interactions

Lateral interactions have also been studied in relation to perceptual learning (Polat and Sagi, 1994b). Perceptual learning, the improvement in perceptual tasks (for example visual discrimination or contrast detection) after prolonged training, is specific for certain characteristics of the stimuli used, like orientation and spatial position.

In 1994, Polat and Sagi applied a perceptual learning paradigm on a lateral masking display configuration where they trained subjects on a contrast detection of a central stimulus with flankers located at different distances relative to the stimulus (0-12λ).

Results showed an increase in interaction range up to twice the different signal wavelengths. The learning effect had a two-stage time course, as previously observed for perceptual learning in texture discrimination tasks (Karni and Sagi, 1993), with the first, slow stage that needs approximately 8 hours to consolidate. Assuming that receptive field size is two times its optimal wavelength (Olzak and Thomas, 1986), at the end of the training session, the trained filter integrates input at distances longer than six times its receptive field size. Authors also reported that longer training periods are proven to be effective for interaction to a distance of up to 20 λ. However, flankers located at separations as small as 2 λ further away from the most distant trained position did not facilitate detection, pointing in the direction of learning localized within a single receptive field size. Polat and Sagi (1994b) then tested the learning effect for configurations that are proven to produce only slight interaction (Polat and Sagi, 1994), such as non-collinear configurations. Training with diagonally oriented stimuli and flankers presented in horizontal configurations did not show any learning effect, whereas the same stimuli, in diagonal, collinear configurations, showed a positive learning effect....?. Consequently, learning took place for configurations in which the target and flankers were aligned along their local orientation, but not when local orientation was 45° away from the global orientation, indicating that practice can only improve the efficacy of preexisting connections. The effect of range interactions

increment was specific for eye, orientation, spatial frequency andretinotopic location, suggesting that learning takes place at the early levels of visual analysis (Ahissar and Hochstein, 1993; Fiorentini and Beradi, 1980; McKee and Westheimer, 1978; Ramachandran and Braddick, 1973; Poggio, Fahle and Edelman, 1992; Karni and Sagi, 1991). In the early stages of cortical processing, interactions are mainly local (Rubenstein and Sagi, 1990; LeVay, 1988; Gilbert and Weisel, 1979; Ts'o and Gilbert, 1986; Mallach, Amir, Bartfeld and Grinvald, 1992), so the modulation in contrast sensitivity could be due to an increase in the range of connectivity between local retinotopic units, either by strengthening of direct long-range connections, or by increasing the efficacy of signal transmission through a cascade of connections. The hypothesis that the reported perceptual enhancement is due to long-range, direct connections led the authors to test a type of training specific to larger distances. However, training using only large separations between target and flankers did not produce contrast threshold reduction. On the other hand, using the whole range of short, medium and large separations led to enhancements at large separation. In conclusion, Polat and Sagi (1994b) proposed that the effect needs a form of integration over the whole range of distances and that training on an incomplete range of distances breaks the cascade of interactions. Moreover, training in which distances were varied within the block produced faster learning, suggesting a time scale of integration for learning. The need for intermediate distances in the training for long range enhancement supports their role as a plausible part of a chain of interactions from near to far connections. In this theorethical? framework, perceptual learning increases the strength of preexisting connections, aligned along the orientation for which the filter is selective and orthogonal to it. These connections could be strengthened only if a specific pair of connected filers, along the chain, is activated within a certain time. Enhancement effect is disrupted when just one of the filters is activated. These learning constraints are consistent with the Hebbian rules but with different (slower) time scales.

Polat and Sagi (1994b) suggested that a stimulus would elicit the activation of a filter arranged topographically, producing a corresponding pattern between near locations in the visual field and near filters in the cortex. The stimulus can activate a filter that transmits an attenuated signal to adjacent filters. This signal can elicit a filter's response in the nearby filters (at distances up to 4λ), but not in distant regions in untrained conditions. If the receiving filter was previously stimulated by another stimulus within a critical window, there is an enhancement in the connections' efficacy, whereby the filters are more likely to be activated by proximal filters. This increased internal signal can be trasmitted successfully through the improved connection between distanct mask-activated filters and the target filter. If the neighboring filter is not activated, the efficacy is reduced. On the other hand, when only a limited number of stimuli are presented, there is a reduction in efficacy of connections between activated filters and their nonactivated neighbors. This reduced efficacy decreases the capacity of the chain to transmit signals between filters across multiple connections, provoking a lack of efficacy across connections between mask-activated sites and target-activated sites. The data presented by Polat and Sagi (1994b) point out the presence of a processing stage in the visual analysis path in which most connections are local but dynamic so as to generate complex patterns of activation that shape the global visual perception. Chains can be expanded and activity may be transmitted and increased when the corresponding filters are stimulated, providing in turn a mechanism for the observed enhancement in the detection of closed figures (Kovdcs and Julesz, 1993). In 1997, Adini, Sagi and Tsodyks applied a perceptual learning paradigm on a lateral masking configuration in which the target was surrounded by multiple flankers located at 2 λ, showing an increase in the range and efficacy of these inhibitory modulations (Adini, Sagi and Tsodyks, 1997). Subjects who did not practice the configuration, increasing the number of flankers beyond two or four (one or two for each side) did not produce modulation of contrast thresholds. Subjects who did practice the configuration, by increasing the number of flankers, produced a non-monotonic effect on threshold: thus adding flankers

reduced the facilitation, while adding even more flankers restored it. This evidence suggests the development of lateral inhibition between adjacent units responding to the high-contrast flankers. These effects appear specific for the configuration: collinear stimuli did not produce inhibition in the first stage of training, while parallel stimuli produced strong inhibition. Training equalized inhibitory effects along these two cardinal directions. Practice increased lateral inhibition and moreover increased facilitation of target detection by neighboring flankers, possibly as a result of reduced inhibitory modulations from flankers to target.

3. Lateral interactions in the periphery of the visual field

Few studies focused on the analysis of lateral interactions in the periphery of the visual field. In 2005, Shani and Sagi conducted a series of experiments in order to investigate this modulatory phenomena at the periphery of the visual field.

Previous studies with electrophysiological recordings in monkeys and cats showed collinear modulations in the extra-foveal regions (Kapadia et al., 1995; Polat et al., 1998), of up to 10° of eccentricity, but any psychophysical evidence for collinear facilitation in humans are reported with stimuli presentation at 3-4° (Williams and Hess, 1998; Zenger-Landolt and Koch, 2001). Assuming that collinear facilitation is based on lateral interactions, this lack of evidence for facilitatory effects could suggest a different network of connections for the periphery respect to the fovea.

However, this interpretation is challenged by anatomical and psychophysiological findings from cats and monkeys, showing that long-range lateral connections are present also in cortical areas that represent the periphery (Gilbert and Wiesel, 1989; Malach, Amir, Harel, and Grinvald, 1993; Ts'o, Gilbert, and Wiesel, 1986). In addition, some studies reported cases of lateral facilitation at the periphery of the visual field in

some observers (Levi, Hariharan, and Klein, 2002; Polat and Sagi, 1994b; Zenger-Landolt and Koch, 2001; Williams and Hess, 1998). This evidence contributes to the idea that the neuronal connectivity in the periphery of the visual field is not structurally different from that of the fovea, so the differences observed in terms of psychophysical results could be due to functional expressions rather than anatomical structure. Assuming that both the areas representing fovea and periphery of the visual field are structurally similar, some factors could contribute to the different modulation of the lateral interactions. Shani and Sagi (2005) proposed that one of the elements which can account for the different lateral modulations between fovea and periphery is the allocation of attention. Indeed, Freeman, Sagi and Driver (2001) showed that in the fovea, allocation of attention can modulate lateral interactions, with different effects on contrast detection for a central target depending on which of two pairs of differently aligned flankers was attended by the subjects: when attention was conducted on collinear flankers, contrast detection was improved, while when attention was allocated on orthogonal flankers, contrast thresholds were higher. So, allocation of attention seems to be a necessary condition for collinear interactions to take place. Considering that the attentional resolution is reduced with the eccentricity (He, Cavanagh, and Intriligator, 1996; Intriligator and Cavanagh, 2001), this could be responsible for the absence of facilitation around 4°, as reported by psychophysical studies. In order to investigate collinear facilitation at the periphery, Shani and Sagi (2005)compared contrast thresholds for collinear and no-flank conditions (Levi et al., 2002; Williams and Hess, 1998; Zenger-Landolt and Koch, 2001). Moreover, they introduced a further condition, for distinguishing the collinear facilitation from a general, unspecific reduction of spatial uncertainty (known to be greater in the pheriphery): primarily, they defined collinear facilitation as "the advantage of the collinear over the orthogonal configuration at threshold," since the spatial uncertainty at the periphery could also be reduced by orthogonal flankers, thus facilitating the detection respect to a non-flanked stimulus. This is an important distinction, since a previous study by Giorgi et al. (2004)

reported collinear facilitation but in comparison with a no-flankers condition, non distinguishing, in this way, between modulation of contrast thresholds due to lateral connectivity in the early visual areas from an unspecific effect of spatial uncertainty reduction. As reported earlier, previous studies with lateral masking showed that 90° orientation difference between flankers and target did not affect contrast threshold for the target (Polat and Sagi, 1993), so the orthogonal condition is a well suited comparison condition. The rationale was that if collinear flankers would produce a reduction of threshold respect to the orthogonal condition at the periphery, then this effect would be orientation specific and attributable to lateral interactions. Authors varied eccentricities of the triplet of stimuli (both with orthogonal and collinear flankers), while measuring contrast thresholds. Results were not consistent among subjects, since different subjects showed reduction of collinear facilitation at different eccentricities, indicating the absence of consistent borders between fovea and periphery. As a general conclusion, for an eccentricity of 4°, contrast sensitivity for orthogonal configuration was higher than that for the collinear. This orthogonal advantage in the periphery could be the product of inhibitory lateral interactions between collinear flankers and targets at 4λ separation or from cross-orientation surround facilitation (Sillito et al., 1995; Levitt & Lund, 1997; Nothdurft et al., 1999; Hupé et al., 2001), Indeed, low contrast flankers produce cross-orientation facilitation in the fovea (Yu, Klein and Levi, 2002). Shani and Sagi (2005) used a separation of 4λ in order to reduce the effect from within the classical receptive field (Zenger and Sagi, 1996)

However, even scaling the stimuli by the cortical magnification factor, according to Rovamo and Virsu (1979), authors did not find collinear advantages in target detection. Since visual cortex units that compute the periphery of the visual field have a larger receptive field respect to the units representing the fovea, Shani and Sagi (2005) hypothesized that distances resulting in facilitation for foveal presentation of the configuration still activate the inhibitory surround of the target's receptive field. In order to verify this hypothesis, Shani and Sagi tested different target-to-flankers

distances. Results showed that at 4°, detection threshold for targets with flankers were lower than threshold for non-flanked target, independently of the orientation of the flankers, pointing at a general, orientation-independent facilitation that could be interpreted as a reduction of spatial uncertainty. Another manipulation carried out by Shani and Sagi (2005) was relative to spatial frequency. Since Tailby et al. (2001) found contrast summation with collinear configuration at 4.8° of eccentricity using Gabor signals with a spatial frequency (SF) of 3 cpd, but not of 6 cpd, they suggested that the discrepancy between 3 cpd and 6 cpd condition is due to low SF tuning of cells at more peripheral sites. In order to test this spatial frequency effect, authors replicated the experiment with 3 cpd of SF instead of 8 cpd. However, decreasing the SF of the Gabor patches did not produce collinear facilitation (relative to the orthogonal condition). At 2 and 4λ separation, orthogonal thresholds were still lower than collinear ones. In this case, the orthogonal advantage is due to increased threshold in the collinear configuration at small distances. Consequently, the orientation-specific increased thresholds are better explained by inhibitory interactions between collinear elements at small distances rather than by cross-orientation facilitation. In all the experiments conducted by Shani and Sagi (2005), subjects were presented with two intervals for each trial, with one of them containing the triplet that could appear at the left or at the right of the fixation point. In a further manipulation, authors modified the display, so that flankers were presented at both sides of the fixation point, with the stimulus presented only on one side. This configuration is more similar to the layout used in previous experiments (Williams and Hess, 1998; Zenger-Landolt and Koch, 2001). However, while the previous experiments adopted a spatial 2AFC, Shani and Sagi (2005) used a temporal 2AFC. Authors also measured contrast thresholds with neutral-orientation flankers (small circles), in order to separate the effect of reduction of spatial uncertainty from the effect of flankers. Subjects showed collinear inhibition at the smallest distances tested (4λ). Thresholds in the orthogonal configuration were similar to the ones in the cue condition, and both did not change for short separations like in the

collinear flankers condition. Authors considered this results as a confirmation for the use of orthogonal conditions as a control for testing lateral interactions in the periphery of the visual field, as they serve as a visual cue. Moreover, it showed that it is not correct to measure lateral interactions in the periphery when comparing collinear and no-flank threshold, like for the fovea: the proper measurement for lateral effects is constrained to comparison between orientation-dependent thresholds. In conclusion, all the experimental manipulation carried out by the author did not lead to collinear facilitation respect to the orthogonal at 4°. In a further manipulation, Shani and Sagi (2005) trained subjects on a contrast detection task with lateral masking, as a way to strengthen or to uncover collinear facilitation in the periphery, in which it is known that inhibition is stronger than at the fovea. However, practice did not uncover collinear facilitation respect to orthogonal condition. Since the allocation of attention seems to be responsible or at least been involved in the lack of collinear facilitation, authors adopted the double task paradigm used by Freeman et al. (2001). The double task consisted in a manipulation of the attention by using a Vernier acuity task, before the detection task. Freeman et al (2001), for foveal presentation of the stimuli, used four flankers around the central target, two collinear and two orthogonal to it. Freeman et al. (2001) then measured detection thresholds for each pair of flankers for which the Vernier task was applied , resulting in orientation-dependent changes: when the collinear flankers were attended to, thresholds were lower than those of the unflanked conditions. Out of this last experiment, authors reported three different types of performances:

1-Attention induced collinear facilitation: detection of the collinear-flanked target was better than detection of the orthogonal flanked target in the double-task, whereas in the single detection task the performances in both collinear and orthogonal configuration were similar.

2- collinear facilitation was present without manipulation of attention. Two subjects showed lower contrast thresholds for the collinear configuration respect to the orthogonal. No difference between single task and double task.

3- attention did not produce facilitation at threshold.

Generally, the average detection thresholds for collinear and orthogonal targets among subjects were not significantly different. However, collinear facilitation was present mainly at performance levels under the Weibull threshold used for the fits, that is 81.6%. The change in steepness and not in threshold does not fit a change in the uncertainty level as an explanation of the effects of the collinear flankers (Pelli, 1985). On the other hand, under the orthogonal configuration, both the threshold and steepness parameters were higher in the double than in the single task, so diminished uncertainty in the double task could account for this difference (but only for orthogonal, not for the collinear conditions where steepness did not change between the single and double tasks). Generally, orienting attention to the flankers revealed collinear facilitation (respect to orthogonal) in some observers, but not consistently in all the subjects. Those who showed facilitation without manipulation of attention may have a correct strategy per se. Shani and Sagi (2005) proposed differences in allocation of attention between fovea and periphery as the reason for the inconsistent outcome among subjects. Moreover, collinear facilitation at 4° in some subjects supports the hypothesis that lateral interactions can be revealed in the periphery similarly to the fovea, consistently with physiological observations.

The reduction of orientation selectivity with the eccentricity could explain at least in part, the reduced peripheral facilitation in the collinear condition relative to the orthogonal. On the other hand, electrophysiological experiments on cats and monkeys confirmed that peripheral cells are still selective for orientation (De Valois, Yund, and Hepler, 1982; Schiller, Finlay, and Volman, 1976; Wilson and Sherman, 1976). Schiller et al. (1976) showed that complex cells exhibit a small decrease in the orientation selectivity with the eccentricity, at a range of 0°-20°. Consequently, in the near periphery, where the stimuli were presented (4°), there are no eccentricity effects expected (De Valois et al., 1982). In any case, the comparison between the orthogonal and the collinear condition assured that the information is processed by different filters

at the periphery. A number of studies showed that orientation information is preserved at the periphery, either by pop-out paradigm (Sagi, 1990; Meinecke and Donk, 2002; Yeshurun and Carrasco, 1998), contour integration (Bonneh and Sagi, 1998, 1999a, 1999b; Hess and Dakin, 1997; Nugent, Keswani, Woods, and Peli, 2003), or orientation discrimination (Parkes, Lund, Angelucci, Solomon, and Morgan, 2001; Sally and Gurnsey, 2003). Moreover, some of these studies clearly suggest the integration of orientation signals in the periphery.

The facilitation in detection could be the product of nonlinear integration from the transducer function around threshold (Legge and Foley, 1980; Usher, Bonneh, Sagi, and Herrmann, 1999; Zenger and Sagi, 1996). Consequently, the flankers shift the operating point of the target filter, producing a change of gain. On this account, the different facilitatory interactions between fovea and periphery could be due to differences in this transducer function. It is plausible to hypothesize that threshold increases at the periphery because of increased noise: thus, the system is not limited by the transducer nonlinearity. A hypothesis is that lateral interactions have different excitation-inhibition balance along with eccentricity, according to the functional necessities and are influenced by the allocation of attention. In any case, while in foveal vision lateral interactions produce facilitation, at the periphery they are mainly inhibitory, consistent with texture processing (Rubenstein and Sagi, 1990). Although the inconsistency among subjects in showing facilitatory collinear interactions in ***the*** the periphery, other studies, focusing on spatial summation, provide evidence for extra-foveal facilitation induced by lateral interactions (Bonneh and Sagi, 1998; Tailby et al., 2001). Bonneh and Sagi (1998) reported that summation decreases when the spacing between the elements increases. However, while experiments with spatial summation, showing the existence of excitatory lateral interactions at the periphery, used stimuli at threshold, the high contrast flankers of lateral masking experiments could produce stronger inhibition. Moreover, the method used by Shani and Sagi (2005) authors could have made it difficult for spotting collinear facilitation (the stimuli were presented randomly on one

side of the fixation point). Moreover, previous studies (Williams and Hess, 1998; Zenger-Landolt and Koch, 2001) used a spatial 2AFC while the authors applied a temporal 2AFC paradigm. There is evidence that the methodology (whether the spatial or the temporal 2AFC) could influence the thresholds (Giorgi et al., 2004). Authors argued that shifting the attention between two spatial positions could have weakened the communication between units, producing in turn no effects of facilitation. Furthermore, Zenger-Landolt and Koch (2001) used 3 λ of target-flank separation with configuration presented a 4°, a distance that could still be inhibitory in most of the subjects. Indeed, the facilitation found by Shani and Sagi (2005) was at 6 □, in the dual task experiment. However, Williams and Hess (1998) reported one subject who showed collinear facilitation relative to no-flankat 6□.

In any case, the facilitation in the collinear configuration, respect to orthogonal in the periphery of the visual field, was not found in previous studies: Polat and Sagi (1994b) reported collinear facilitation at 3° of eccentricity in a side note, while Giorgi et al., (2004) showed collinear facilitation relative to no-flankers condition at 2-6° only when using a temporal 2AFC paradigm (absent with spatial 2AFC). They also reported a high inter-subject variability. Levi et al. (2002) also reported collinear facilitation relative to no flank condition at 5° for one of their subjects (temporal 2AFC). The facilitation was also relative to a parallel arrangement of target and flankers, attributing the effect to lateral interactions. This evidence indicates the possibility of finding collinear facilitation (relative to no-flank condition) in the periphery of the visual field.

What still seems to be a puzzling question is the apparent lack of consistency between human phsycophysics and animal neuroanatomy for lateral interactions. Assuming the similarity in neuronal networks between primates and humans, the low-level initial physiological response of humans should produce contextual facilitation for peripheral stimuli similar to that reported in experiments with primates. Attention could intervene in a later processing stage, influencing the response (at different levels of analysis by using feedback connections) and producing different outputs, as observed in the inter-

individual differences between subjects. On the other hand, there are less differences between humans and primates for foveal facilitation, probably because of a more stable allocation of attention at the fovea. Recently, Lev and Polat (2011) proposed some reasons why previous studies reported inconsistent results regarding lateral interactions in the periphery. Authors suggested, in agreement with Giorgi et al. (2004), that collinear facilitation for peripheral presentation may be sensitive to the procedure used: the 2AFC procedure could produce difficulties in maintaining fixation. Moreover, one of the reasons why peripheral facilitation is not consistent among studies could be due to its orientation-insensitive nature (Shani and Sagi, 2005). Finally, authors stated that maybe the target-to-flankers separations tested in previous experiments (Williams and Hess, 1998; Shani and Sagi, 2005) were not ideal for revealing the facilitation. In fact, larger distances than the ones that result in facilitation for the fovea produced facilitation in the periphery, consistently with magnification factor (Dow et al., 1981; Duncan and Boynton, 2003; Levi, Klein, and Aitsebaomo, 1985). Lev and Polat (2011), by using a yes/no procedure (Polat and Sagi, 2007) and testing larger target-to-flankers distances (7□), reported peripheral collinear facilitation that is orientation-selective, consistent with previous reports on the architecture of foveal lateral interactions (Polat and Sagi, 1993, 1994a). Authors suggested a model accounting for collinear interactions along the entire visual field, both for foveal and peripheral vision. Lev and Polat (2001) stated that suppression takes place when flankers are presented within the same hyper-column as the CRF, while facilitation is the consequence of activation of different hyper-columns. The ideal distance for facilitation is invariant if expressed as the distance between adjacent hyper-columns that are fixed in the visual cortex. They reported that lateral interactions could have their physiological basis in a network of long-range connections between columns with similar orientation preference (Bolz and Gilbert, 1989; Gilbert and Wiesel, 1985; Grinvald et al., 1994; Ts'o, Gilbert, and Wiesel, 1986).The ideal separation for inducing facilitation increases with the eccentricity due to the increasing size of the perceptual receptive field (perceptive field,

PF). This evidence suggests a shift toward lower spatial frequencies activated for increasing eccentricity, consistent with previous data (Gelb and Wilson, 1983a, 1983b; Graham, 1989). Consequently, while the stimuli used by Lev and Polat (2011) appear to be ideal for foveal activation of PFs, in the periphery they may activate PFs of larger sizes. Some authors (Petrov and McKee, 2006; Polat and Sagi, 1993) suggested that lateral masking and crowding are connected: both depend on the target-to-flankers separation, and the effect increase with eccentricity. Lev and Polat (2011) underlined how the target-to-flankers distance must be increased for producing collinear facilitation. Since it has been proposed that crowding depends on the presentation of both target and flankers stimuli within the same "perceptive hypercolumn" (Levi, Klein and Aitsebaomo, 1984), larger peripheral PFs may be presented in one hypercolumn. Lev and Polat (2011) suggested that the reduced collinear facilitation for small distances at the periphery could illustrate that it takes place within the same hypercolumn which represents the dimension of the peripheral PF. Within this theoretical framework, crowding and lateral masking may be influenced by the same lateral interactions.

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Chapter 2

Perceptual learning

As stated in the previous chapter, the whole idea of the primary visual cortex (V1) as a set of independent units, processing single features from restricted areas of the visual field, has advanced. Growing evidence for interactions even at the first stages of visual processing brought to further investigate the relationship between codifying units. These mechanisms of interactions can be considered a way in which the visual system mediates simple context effect with context representing remote image parts. A number of studies (Sagi and Tanne, 1994; Ahissar and Hochstein, 1999; Karni and Bertini, 1997) showed that these early context effects can be modulated by practice, suggesting the possible role of plasticity in low-level visual circuits. The behavioural improvement following repetitive practice on perceptual tasks is called perceptual learning. In her seminal book, *The Principles of Perceptual learning and Development*, Gibson defined perceptual learning as "the increase in ability to extract information from the environment, as a result of practice and experience with stimulation coming from it" (1969). This definition highlights the importance of extracting and selecting information. However, enhanced performance could also depend on other factors, such as information processing or decision making. Studies on perceptual learning point towards understanding the level of processing and the mechanisms responsible for learning in a specific task. Volkman (1858) and Tawney (1897) are among the first who investigated perceptual learning: they found that practice reduced the minimal separation (or JND, just noticeable difference) at which subjects were able to distinguish the spatial location of two points touching their skin.

Impressively, in some areas of the skin, hours of practice reduced thresholds to as low as 1% of the initial separation. Authors suggested that this improvement was mediated

by an unknown, high-level neural mechanism. However, while for some type of tasks an improvement, sometimes considerable, is observed, for other tasks it seems that practice does not ameliorate performance. Johnson and Leibowitz in 1979 reported that practice in discriminating between simple gratings did not produce improvement in resolution with foveal stimuli presentation, but it did yield a considerable improvement with stimulus presentation in the periphery of the visual field.

On the other hand, complex grating discrimination is sensitive at improvement after learning, both in central and foveal vision (Fiorentini and Berardi, 1980, 1981).

The different effects of learning on these two distinguishable tasks are most probably due to the diverse every day life experiences of the participants undertaking these tasks. Some tasks are practiced more than others, so a certain degree of learning already occurred for some of the tasks.

For example, discrimination of simple gratings at the fovea is an important ability, therefore information processing for this type of stimulus is likely to be already fully developed, while for resolution at the periphery of the visual field (usually implicated in the phenomenon of foveation) there may still be a room for expressing its potentiality. Consistently with this hypothesis, resolution for stimuli with horizontal or vertical orientation is considerably better than resolution for oblique orientation, since it is less relevant in everyday life. Confirmations come from experiments showing that practice can improve performance for oblique orientation but not for horizontal or vertical (Vogels and Orban, 1985): training can improve performance only when the task has not been already optimally trained.

Moreover, perceptual learning is inevitably constrained by the anatomical structure of the neural network on which it acts. Taking peripheral vision as an example, practice cannot ameliorate it to the level of foveal vision, because there are basic differences in the cortical magnification factor, that is the number of neurons devoted to compute and represent different portions of the visual field. Given these anatomical differences, Vogel and Orban (1985) suggested that even extended practice cannot produce such an

improvement to eliminate the gap between foveal and peripheral vision. On the other hand, more recent results suggest that such improvement may require extensive long-term learning, as indicated by results showing improved contrast sensitivity and integration time in video gamers (Li, Polat, Makous, and Bavelier, 2009). While Vernier acuity shows enhancement due to practice, Landolt C and two-line resolution thresholds do not improve. Westheimer (2001) suggested that in the absence of learning, the process is probably of a more primitive type, almost sensorial in its origins. This evidence suggests that the human visual system has expertise in some basic tasks but they cannot further improve. This expertise is subjects to inter-individual differences, so in case of low baseline performance, there is a possibility to observe some learning. For example, in the learning of a hyper acuity task, Fahle and Henke-Fahle (1996) found large variability among subjects, which they accounted for by the different baseline performances of the subjects. A similar effects was reported by Dosher and Lu (2005) in a contrast-detection task.

2.1 Neural plasticity and perceptual learning

When there are the right conditions for improvement, it has been shown that this can last for weeks or even months. Karni and Sagi (1991, 1993) described two stages of learning in a texture discrimination tasks. In the first one, the improvement is fast, occurring during the first session of practice, while in the second, slower stage, the improvement is between sessions and takes place hours after the sessions terminate. According to Karni and Sagi (1991, 1993), the first, fast stage reflects the improvement of task-specific strategies for solving the perceptual problem, while in the second, slower stage, long-term structural modifications of perceptual modules take place, consolidated through sleep. Consistently with this hypothesis is the evidence that sleep

deprivation interferes with this second stage of learning (Cipolli, Campana, Campi, Mattarozzi, Mazzetti, Tuozzi, Vandi, Vignatelli and Plazzi, 2009; Stickgold, James and Hobson, 2000), and that both slow wave sleep (SWS) and rapid eye movement (REM) contribute to consolidating experience-dependent neuronal changes into a form that supports improved task performance (Stickgold, Whidbee, Schirmer, Patel, Hobson, 2000). Another experiment pointing out that structural modifications of basic perceptual modules are a neural correlate of learning is reported by Walsh, Ashbridge and Cowey (1998). The authors showed that transcranial magnetic stimulation (TMS) applied over the right posterior parietal cortex during a conjunction search task produced different effects depending on the novelty of the stimuli used: Results indicated that performance was impaired by TMS when the stimuli were novel and required a serial search strategy, but not after the task had been learned. This could be considered as an evidence of plasticity in the underlying neural network, possibly a modification within areas in the ventral stream, which no longer need the involvement of focal attention to perform the task, once it has bee learned. Neural plasticity in the primary visual cortex is the subject of a contemporary debate among visual scientists (Wandell and Smirnakis, 2009), as well as its role in perceptual learning. In the psychophysics field, the specificity of the stimulus is considered the main indicator of the level of processing at which learning takes place. This statement is based on current models of the visual system and on the processing stages assumed. In general, the first, low-level stages of processing in the visual system compute simple feature such as local contrast, orientation, color, motion, while higher levels of analysis take into account a localized spatial region for recognizing objects, so that higher level processing read out the outputs of the early stages (Dosher and Lu, 1999). This type of structure, with different stages and hierarchical organization, is theoretically fascinating and contributed to change the interpretation of area V1 that become the cortical area that redistribute visual information to the higher level regions, that rely on these inputs for creating representation of the world (Wandell and Smirnakis, 2009). More recent research has

challenged the rigid view of low-level processes as being local and independent by showing the existence of long-range interaction between detectors as having the same orientation preference (Polat and Sagi, 1993), with brain correlates found in the primary visual cortex (Gilbert, Li, and Piëch, 2009; Tajima, Watanabe, Imai, Ueno, Asamizuya and Sun, 2010). Moreover, a number of studies (Li, Piëch, and Gilbert, 2008b; Offen, Schluppeck, and Heeger, 2009) showed task dependent modulation of V1, subtending top-down activity. Perceptual learning involving target identification tasks has shown to be specific for retinal position and orientation (Nazir and O'Regan, 1990). Another way to find the different levels of processing is to use tasks constrained by limitations of the visual processing, known to have functional-anatomical correlates. In other word, taking into account the correspondence between cerebral anatomy and visual functions. On the other hand, the aforementioned anatomical-functional mapping does not always suit with most behavioral experiments. Performances at hyper-acuity levels, obtained following an extensive training (Fendick and Westheimer, 1983), need the access to low-level neuronal representations, where the details necessary for reaching this level of performance are located. On the other hand, Poggio, Fahle and Edelman (2002) hypothesized that in this case, learning can be explained by a process of integration of the input in the low-level representation, that is task specific.. Indeed, studies on hyper-acuity report task specificity in learning (Fahle and Morgan, 1996), pointing out that the cause of learning is not a general improvement of spatial resolution. Psychophysical evidence indicates a distinction between tasks in which the observer's attention is focused and tasks in which it is distributed along the visual field. Most of the tasks studied in perceptual learning are of the former type, like orientation and contrast discrimination, in which observers can focus on a limited portion of the visual field. In the latter type of tasks, the target is shown among a number of distractors, so they are forced to use distributed attention, like in texture segmentation. Bergen and Julesz, in 1983, showed that with some combinations of the texture elements, observers performed excellent segmentation, independently from the number of elements present,

as it was a parallel search. The combination that led to this rapid segmentation was characterized by a target-background difference in some basic low-level features, such as orientation. In this condition, it seems clear that the searching is performed by a parallel network of units, having receptive field properties similar to those of the V1 area (Knierim and van Essen, 1992; Li, 2002; Rubenstein and Sagi, 1990; Tajima et al., 2010). On the basis of these observations, the evidence from perceptual learning in orientation-based search (Ahissar and Hochstein, 1993), texture segmentation (Karni and Sagi, 1991) and contour integration (Gilbert, Li and Piëch, 2009) point at modification of low-level visual process, without the intervention of attention (Braun and Sagi, 1991). All these studies showed specificity for location and orientation of the stimulus used, moreover they showed partial selectivity for the trained eye (Ahissar and Hochstein, 1996; Karni and Sagi, 1991). Eye selectivity was reported only in the second stage of learning, and showed slow time course and higher specificity for the characteristic of the stimulus (Karni and Sagi, 1993). Specificities were also observed for the "focused tasks", in particular location and orientation, and in some case eye selectivity (Fahle, 2004). In general, results support the hypothesis of neuronal plasticity that takes place at low-level stages of visual analysis.

2.2 Mechanisms underlying perceptual learning

Even if it is well known that practice can improve performance in visual tasks, the underlying neuronal mechanisms involved has not been discussed in the early studies on perceptual learning, Experimental reports from the 60s and the 70s frequently mentioned that practice trials were given to the experimental observers to familiarize them with the task, but only a small number of reports documented the resulting effects. Growing discussions in the following years brought on investigations on the mechanisms underlying perceptual learning and attempted to shed light on questions like the distinction between changes in the representation stages (stimulus related) or in

the decision stage (task related). Different theories have been developed to describe these mechanisms:

1-learning reduces the necessity for attention.

Treisman and Gelade (1980) stress the importance of attention in feature binding during object identification. Learning could possibly reduce the amount of attention necessary to perform the task, shifting from an effortful process to an automatic (almost parallel) one. The study of Ellison and Walsh (1998) is consistent with this idea: observers' performance in a conjunction search task becames parallel after intense practice. Furthermore, TMS studies showed the involvement of the right parietal cortex, known to play a role in attentional tasks, in novel conjunction search tasks, but not in feature tasks or learned conjunction search tasks (Ashbridge, Walsh and Cowey, 1997; Walsh, Ashbridge and Cowey, 1998). Creation of specific complex feature detectors (Laberge, 1976; Campana and Casco, 2003) or direct link between stimulus detection and subject's response, skipping the decision-making stage (Shiffrin and Schneider, 1977) have been proposed as an explanation for the increased automaticity after learning. Treisman, Vieira and Hayes (1992) observed a reduction in search time slope (from 100 to 20 ms/item) after extensive practice. However, Cheng (1985) suggested that the slope reduction could reflect a shift in strategy rather than increased automatization.

2- learning produces "enrichment" and "differentiation".

As proposed by Gibson (1955), it is based on the assumption that improved discrimination after learning can be achieved by "enrichment" and "differentiation". Enrichment is related with early stages of visual analysis and may be the product of increased connections between detectors; while differentiation takes place at the decision stage and involves a selection of information by strengthening the most informative input connections and discarding the others. According to this model, learning would be specific only to task relevant features. However, Treisman, Vieira

and Hayes (1992) found that learning was specific not just for task relevant feature, but also for target location and texture.

3- learning increases speed and efficiency of ingrained processing

another interpretation of perceptual learning effects is that it improves pre-existing processing. Visual search training would reduce the amount of time necessary for detection increasing target discriminability respect to the background (Treisman and Sato, 1990; Wolfe et al., 1989), by shifting search from single elements to groups of elements (Casco, Campana and Gidiuli, 2001; Humphreys and Muller, 1993), or by substituting a process-based mechanism with a memory-based mechanism (Logan, 1988).

4- Reverse hierarchy theory

Ahissar and Hochstein (1997, 1999, 2000) reported that increasing the task difficulty reduced the attentional window and increased the specificity of learning. They Authors suggested that spatial attention and learning are primarily directed to the highest levels of the hierarchy, where neurons respond to global properties of the visual stimuli. While for easier tasks this is sufficient, more demanding conditions require higher mechanisms to shift attention and learning to lower levels. If the direction of information is bottom-up, guidance for the level of processing (and learning) is top-down. This hypothesis can solve the lack of consistency between the study of Fiorentini and Berardi (1981) on phase discrimination, in which learning exhibited fast saturation and interocular transfer, as well as the study of Ball and Sekuler (1987) on motion discrimination, where learning was reportedly slower, with only partial interocular transfer. The different levels of difficulty may have shifted attention (and thus learning) to lower level mechanisms in the first case, and to intermediate levels in the latter case. On the other hand, Lu and Dosher (1999) measured perceptual learning by varying the amount of external noise associated with the stimulus, for testing the type of plasticity in the

visual system. Performances were improved after learning both in high external noise conditions (where the limiting factor is external noise) and low external noise conditions (where the limiting factor is internal noise). Lu and Dosher (1999) suggested that in the first case there is a mechanism of external noise exclusion, while in the second case there is an enhancement of stimulus discriminability due to internal noise reduction. Consequently, learning might take place at the level of basic visual channels, reflecting plasticity in their relative activity.

2.3 Physiological correlates of perceptual learning

Despite Hubel and Wiesel (1970) suggested that plasticity at early stages of visual cortex is not retained after an initial period, further studies on sensory deprivation (Gilbert, 1993; Merzenich, Kaas, Wall, Nelson, Sur and Felleman, 1983) questioned this statement. In deprived animals, the dimension of the receptive field of visual neurons in the sensory deprived regions increased, including the surrounding region of the visual field. Consistently, in other studies (Fregnac, Shultz, Thorpe and Bienenstock, 1992; Shultz and Fregnac, 1992) it was reported that the preference of single units could be modified in the direction of initially non-preferred stimuli by using external stimulation concomitantly with visual presentation. Ocular dominance and orientation have been shown to be sensitive to this modification. Considering this as a possible mechanism of plasticity at the basis of perceptual learning, a question that could arise is what would produce the increased activation under normal, non-externally stimulated, conditions. A possible explanation could be selective attention, that increases the representation of relevant stimulus parameters or, alternatively, differentiate and select the more adapt neuronal population. Crist, Li and Gilbert (2001) investigated the representational changes underlying perceptual learning in the visual system. They reported specificity of learning for spatial position and orientation in monkeys trained on bisection

discrimination task. This high specificity suggests possible changes at the stage in which units responds selectively to these features, probably V1. Conversely, these authors did not find any increase of the region representing the trained area of the visual space in V1. Moreover, the receptive fields of V1 units responding to the trained stimulus did not change. V1 units are influenced by stimuli located outside their classical receptive field, with a modulation than could be excitatory or inhibitory, depending on the spatial relationships between the stimulus located within the receptive field of the V1 unit and the stimuli located outside. As reported in the previous Chapter, firing rate of a neuron responding to an oriented bar located within its classical receptive field can be modulated? by positioning another stimulus outside the receptive field of the given neuron (Crist et al., 2001). For example, firing of a neuron responding to an oriented bar (target, placed within its classical receptive field) can be decreased by placing another bar (flanking, parallel to the first one) just outside the neurons receptive field. Crist et al. (2001) found that after learning the bisection task the effect of a flanking bar was asymmetrical. The neurons firing could be increased or decreased, depending on which side of the target bar the flanking bar was placed. Moreover, the effect was specific to the trained task and configuration. For instance, when a flanking bar was introduced in a control fixation task, it had little effect on firing rate. Plasticity in V1 thus seems to be governed by complex stimulus parameters such as task-dependence, probably modulated by top-down influences and mediated by feedback connections (Gilbert, Ito, Kapadia and Westheimer, 2000; Crist et al., 2001). Other studies (Kubota and Komatsu, 1985; Mitz, Godschalk and Wise, 1991; Vogels and Orban, 1992) examined learning effects by recording neuronal responses in higher cortical areas (inferotemporal, premotor, and frontal cortex). In these studies specificity has been found for task attributes but not for stimulus attributes. Task related effects found at higher cortical areas and stimulus specific effects found in lower cortical areas may reflect the hierarchy of processing governing the visual stream. Perceptual learning seems to modulate EEG responses both within sessions (Casco, Campana, Grieco and

Fuggetta, 2004; Skrandies and Fahle, 1994) and between session (Pourtois, Rauss, Vuilleumier and Schwartz, 2008). Pourtois et al. (2008) reported that early EEG component, like C1, indicating activity in V1, were modulated by learning in texture discrimination task. Top-down processes in V1 are assumed to take place only 100 ms after the stimulus onset (Li, Piech and Gilbert, 2004), so early modulation (<85 ms) reported by Pourtois et al. (2008) indicates that learning induces changes in V1. Another study investigated the connection between visual performance and visual event-related potentials (ERPs) in a backward-masked texture segmentation task (Censor, Bonneh, Arieli and Sagi, 2009). Authors found practice-dependent temporal interactions between early components (N1) of the ERPs corresponding to the target and the mask. These interaction correlated with reduction in performance and might be used to predict the threshold of the subjects. Reportedly, training reduces temporal interactions between consecutive stimuli, probably through increase of target processing in the early visual areas.

2.4 Specificity of perceptual learning

Vision science applied the perceptual learning paradigm to a number of different tasks, such as detection and discrimination of visual gratings (Fiorentini and Berardi, 1980 1981), stimulus orientation (Vogels and Orban, 1985; Shiu and Pashler, 1992; Fahle, 1997), motion direction discrimination (Ball and Sekuler, 1982, 1987) and hyperacuity tasks (Bennet and Westheimer, 1991; Beard, Levi and Reich, 1995; Fahle and Edelman, 1993; Fahle, Edelman and Poggio, 1995; Saarinen and Levi, 1995). Experiments on visual searching tasks also showed perceptual learning effects (Karni and Sagi, 1991, 1993; Sireteneau and Rettenbach, 1995, 2000; Ahissar and Hochstein, 1993, 1996, 1997, 1998, 2000; Ellison and Walsh, 1998; Casco, Campana and Gidiuli, 2001).

These effects can last for weeks or months, and are specific for the basic features of the trained stimuli. When tested with stimuli of different features, the level of performance was similar to the pre-training condition. The specificity of the learning is indicative of the processing stages underlying the enhanced performance. For example, if the learning is specific for the trained orientation (Ahissar and Hochstein, 1996), than the stage at which the learning takes place cannot be located earlier than the orientation selective units (i.e. before V1). Similarly, if the enhanced performance is specific to spatial frequency (Fiorentini and Berardi, 1980, 1981), or to stimulus size (Ahissar and Hochstein, 1993), then learning must take place before high visual areas (such as IT), where there is abstraction of these specific properties (Gross, Rocha, Miranda and Bender, 1972; Gross and Mishkin, 1977). The constant increase in the dimension of the receptive field of the units along the pathways of visual analysis (with units at higher level areas having a receptive field extending to nearly a whole hemifield; Gross and Mishkin, 1977) sets the specificity in the spatial domain as an important indicator in localizing the site at which learning takes place. On the other hand, interpretation of spatial resolution data is not always straightforward, in terms of locating the anatomical site in which plasticity takes place. Moran and Desimone (1985), in a study with monkeys, reported that spatial tuning can be dynamically modified by the context. Authors showed that receptive fields of V4 and IT units can shrink when monkeys undergo to a task requiring selective attention. One of the strongest evidence for low-level occurrence of plasticity (at the level of V1) is the ocular specificity, as reported by Karni and Sagi (1991). In V1, in fact, there are still units responding separately to input from either eyes. A number of studies, using different stimuli configurations and tasks, reported different sites for the plasticity. Poggio, Fahle and Edelman (1982) identified the learning of orientation discrimination at the level of orientation specific cells, while Karni and Sagi (1991, 1993) located the learning of texture segregation at the level of mechanisms dependent on retinal input. On the other hand, Siretenanu and Rettenbach (1995, 2000), using feature search tasks, reported that learning was not specific and

transferred to different stimuli, indicating a higher level site for the learning of these stimuli. In this case, the learning is not related to an improvement for specific features, but it is a general improvement in search strategy. However, the effects reported by Sireteanu and Rettenbach (1995, 2000) were referring only to feature, parallel search, and trials with no target displayed (target absent trials), and the search was serial. Therefore learning generalized to these particular stimuli, and could not be applied to other search conditions. In fact, Ellison and Walsh (1998) reported an asymmetry of transfer between feature and conjunction searches. Learning for pop-out search did not transfer to a difficult conjunction search, while learning transferred from conjunction search tasks to pop-out search. Authors suggested that learning in visual search is specific, and that the mechanisms underlying serial search contain all the elements of processing needed for pop-out search. Ahissar and Hochstein (1996) provided data supporting high specificity of learning for feature search. They studied specificity of learning in preattentive and parallel texture segregation task based on orientation gradient. Their results showed strong selectivity for position, size and orientation of textural elements, so Ahissar and Hochstein (1996) suggested that learning with these stimuli took place at early stages of processing, in the striate or extrastriate visual areas where there are units responding to these stimulus characteristics. These results are similar to the ones of Karni and Sagi (1991, 1993), in which they found two stages for perceptual learning in a texture discrimination task. In the first one, the improvement is fast and occurs within a single session and is specific for some stimulus features but not for the trained eye. In the second one, improvement is slow and between sessions, and needs several hours to consolidate. This stage is specific for the trained eye (not transferring to the untrained eye) indicating the involvement of earlier stages of processing. Clearly, if perceptual learning is the product of the tuning of units activated at the early stages of cortical processing, then it should be specific for the features to which these units respond. In the early levels of visual processing, these features are orientation, ocular dominance (at least at the level of initial cortical cells in layer IV),

spatial frequency, length and position. Consequently, learning of visual search could depend on different processes depending on the task and the stimuli rather than being the product of a single mechanism. Other authors focused on the role of attention in perceptual learning. Ahissar and Hochstein (1997) investigated whether training a task in which subjects had to attend global aspects produced learning in another task where previously unattended, local aspects became relevant for the task. With same stimuli and difficulty level, these authors did not find any transfer across tasks. Ahissar and Hochstein (1997) suggested that subjects have to selectively attend to features of the stimulus and perform the task in order to reach an improvement in performance. Rubin, Nakayama, and Shapley (1997) reported that few examples of a stimulus to be discriminated are sufficient for promoting an improvement in performance with more difficult stimuli. the authors only found an improvement in performance when the stimuli were easy whereas no improvement was seen in response to difficult stimuli. Moreover, Ahissar and Hochstein (1997) tested the effect of a single easy trials comparing subjects who received the easy trials before performance and subjects who did not. All the subjects exposed to the easy trials showed improvement, while most of the subjects who did not see the easy trials did not improve in performance. This effect, called “abrupt learning”, or “eureka effect”, seems to be specific for basic features of the stimulus, challenging the distinction proposed by Karni and Sagi (1991) between two stages of processing for learning (whereby the first stage - fast learning - should only reflect an improvement in strategy).

2.5Neural modelling of Perceptual Learning

Neural models for perceptual learning are divided in two general types: Feed-forward and Feedback models. Most of the results coming from perceptual learning experiments

can be interpreted according to a feed-forward models without recurrent interactions (Dosher and Lu, 1999; Eckstein, Abbey, Pham and Shimozaki, 2004; Poggio et al., 1992). These type of models are characterized by a cascade of stages of processing, with an input layer at the start and a decision unit at the end. This decision unit has the role of integrating weighted inputs from units located at lower level and producing a response, with output levels corresponding to the behavioural responses. Perceptual learning in these models can be introduced using a teaching signal applied in order to modify the input weights for the decision unit using associative learning rules (Poggio et al., 1992). Specificity for stimulus and task can be modeled by introducing new learning modules (referred to the decision or pre-decision stages), designed for producing optimal performance on new tasks. Feedback for decision errors is important but not crucial in these types of network (Herzog and Fahle, 1997, 1999; Poggio et al., 1992). Alternatively, it can be produced internally, on the basis of evaluation after obvious discriminations (Fahle and Edelman, 1993; Herzog and Fahle, 1998). Another possibility is to implement learning of re-weighting by introducing a feedback-dependent bias to the decision unit (Petrov, Dosher and Lu, 2006). This bias relies on information acquired by the subject only after the production of a response, and requires the input to persist until the decision is taken, indicating a temporal window of few seconds. Polat and Sagi (1994b) proposed a type of associative learning with a similar time scale in their study on lateral interactions, where there is evidence for long-term persistence of sub-threshold effects (Tanaka and Sagi, 1998a, 1998b). Sometimes learning depends on aspects not intrinsically related to the trained task, such as task-irrelevant stimuli surrounding the target (spatial context) or stimuli presented before the target (temporal context). These types of effects are better explained by theories assuming feedback (recurrent) networks. In these networks, learning does not require external feedback. Its implementation often relies on associative rules that act on the connection strength between pairs of units according to activity correlation. Anatomical evidence proves that long-range horizontal interactions are present in all the cortical

areas, including the visual cortex (Gilbert and Wiesel, 1983; Rockland and Lund, 1983) and can be modulated by perceptual learning (Gilbert et al., 2009). In psychophysical studies, as reported in Chapter 1, similar long-range interactions have been reported between laterally displaced Gabor patches (Polat and Sagi, 1993; 1994a). Polat and Sagi (1994b) reported an increase in the range of these lateral interactions, interpreted on the basis of enhancement efficacy of pre-existing connections, producing a cascade of progressive units activation. This interpretation is consistent with evidence of improved contour integration after training (Kovàcs and Julesz, 1993; Kovàcs, Kozma, Feher and Benedek, 1999). In 2009, Li, in 2002, applied a V1-based model of visual segmentation (Li, 2002), using inhibitory lateral interactions to model learning in texture tasks (Ahissar and Hochstein, 1996; Karni and Sagi, 1991), successfully replicating results from the literature. A hypothesis on learning in texture-discrimination tasks states that it involves strengthening of inhibitory interactions between neighboring cortical units responding to the oriented texture features, consistent with the experimental evidence showing specificity of learning to background orientation (Karni and Sagi, 1991). This model demonstrates that behavior depends on spatial characteristics such as line length and density (Sagi, 1990; Sagi and Julesz, 1987). Contextual effects reported for contrast discrimination (Adini, Sagi and Tsodyks, 2002) supports a V1-like model that assumes cortical columns composed by interconnected excitatory and inhibitory units (Wilson and Cowan, 1972). Experimental evidence from contrast discrimination with localized Gabor stimuli shows stable contrast-discrimination thresholds. On the other hand, the concomitant presentation of high-contrast Gabor flankers produced learning, reducing contrast thresholds, even when flankers were removed. Adini et al. (2002) proposed that performance in contrast discrimination tasks depends on the balanced activity of excitatory and inhibitory units. The balance, preserved by activity-dependent synaptic connections regulated by hebbian-like learning rules, is unchanged when the network is locally activated but is disrupted when activation expands to lateral inputs. As a consequence, contextual information produces learning within local networks.

According to this model, lateral interactions are not modulated via changes in weights of lateral connections, but through modifications of excitatory and inhibitory weights within each column. Recently, it has been proposed that plasticity in the visual cortex is managed by the balance between excitatory and inhibitory interactions (Morishita and Hensch, 2008), with reduced intra-cortical inhibition accounting for cortical plasticity in adults (Harauzov, Spolidoro, DiCristo, De Pasquale, Cancedda, Pizzorusso, Viegi, Berardi & Maffei, 2010; Sale, Maya, Vetencourt, Medini, Cenni, Baroncelli, De Pasquale, 2007)

2.6 Critical period

The idea behind the critical period is that some sensorial functions are acquired during the development and, after a certain amount of time, cannot be modified. Studies on cats revealed that cortical unit properties, such as ocular dominance, can be shaped by experience only within a certain period after birth (Hubel and Wiesel, 1970; Wiesel and Hubel, 1963). It seems that for different functions there are separate time windows: for example, stereo vision seems to mature early after birth (3-4 months, Braddick, Atkinson, Julesz, Kropfl, Bodis-Wollner and Raab, 1980), whereas contour integration consolidates later (>15 years, Kovàcs, 2000). Different authors focused on the possibility, for perceptual learning, to be effective after the development of the visual system. A possible test-field concerns visual pathologies in which visual development is abnormal. Shina and colleagues (Bouvrie and Shina, 2007; Ostrovsky, Andalman and Shina, 2006) reported the case of a woman born blind following congenital cataracts, removed when she was 12. On testing her vision 20 years later, they found low visual acuity but good image segmentation and recognition. This data testifies that the visual system maintains its plasticity even after years of deprivation. Amblyopia, a visual impairment characterized by abnormal development of the visual system, has recently been studied with perceptual learning procedures. While absence of visual inputs during

development could not affect the visual cortex (Mitchell and Sengipiel, 2009), abnormal visual experience could produce depression of some functions, such as an increased inhibition in the visual cortex, as reported for rats monocularly deprived during the critical period (Maffei, Nataraj, Nelson and Turrigano, 2006). Recently, some studies provided evidence for plasticity in adult, amblyopic rats that restored their ocular dominance and improved their visual acuity after complete deprivation (He, Ray, Dennis and Quinlan, 2007). Harauzov and colleagues (2010) .proposed that the increased inhibition in amblyopia is the reason for limited plasticity in adults.

Perceptual learning treatments have proven to be effective in improving visual abilities in adult amblyopes (Levi and Li, 2009a, 2009b; Levi and Polat, 1996; Levi, Polat and Hu, 1997; Pennefather, Chandna, Kovàcs, Polat and Norcia, 1999, Polat, 2009). These studies showed that learning transferred to other visual abilities, supporting the idea of greater potential for visual plasticity in amblyopes (Astle, Webb and McGraw, 2010; Huang, Zhou and Lu, 2008). Polat and colleagues (2004) trained a group of amblyopic patients in contrast detection with flanked Gabors stimuli, and reported improvements in the trained tasks which also transferred to visual acuity. Polat et al. (2004) suggested that lateral interactions in the primary visual cortex of amblyopes are impaired, as supported by experimental evidence on the absence of collinear facilitation (Polat and Sagi, 1993; Polat and Sagi, 1994a) in amblyopes (Polat, Sagi and Norcia, 1997). Moreover, lateral interactions in the amblyopic eye were extremely inhibitory and reduced after training (Polat et al., 2004).

2.7 Conclusion

Many authors devoted attention to perceptual learning, studying different aspects and analyzing it at different levels. In recent years, research focused on investigating the underlying, perceptual mechanisms of learning and simultaneously using the perceptual

learning procedures to study learning and memory processing. The experiments reported showed that experience with visual stimuli produces long-lasting modifications in the perception of these stimuli, suggesting that the visual system undergoes an experience-dependent plasticity. Recent studies showed that learning depends on temporal and spatial context, providing a more precise identification of the neural networks involved in learning and the rules that govern it. A number of studies have shown that, in some conditions, learning can generalize and transfer to untrained stimuli and task. One of the most interesting perspective in perceptual learning concerns studies on populations affected by visual deficits due to abnormal development, such as in amblyopia: when trained with some specific tasks, their visual abilities improve. This evidence support the idea that visual development can still be active after the critical period has ended, and that perceptual learning, in some conditions, could be used as a treatment to overcome visual deficits.

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Chapter 3

Experiment 1: Investigation on lateral interactions at the periphery of the visual field, perceptual learning modifications and transfer of learning to other visual functions

In Experiment 1, we investigated lateral interactions in the near-periphery, describing the type of modulation (inhibitory vs. facilitatory) for different distances between target and flanker stimuli. Moreover, we aimed at verifying if a perceptual learning paradigm could modulate inhibitory lateral interactions and whether learning could be transferred to higher-level lateral visual functions, as already reported for foveal presentation (Polat, Ma-Naim, Belkin and Sagi, 2004, Tan and Fong, 2008). As stated in the Chapter 1, models of early visual processing rely mainly on the idea that the visual input is analyzed by mechanisms which respond both locally and independently to a specific range of orientations and spatial frequencies (Hubel and Wiezel, 1963; Campbell and Robinson, 2008; De Valois and De Valois, 1988). In recent years, a number of psychophysical and physiological studies have shown that despite these mechanisms are assumed to be local and independent, they interact. In fact, a significant number of studies have supported these findings by showing that the contrast threshold for detecting a target (example, a Gabor patch or a bar) was modulated if the target was flanked by two high-contrast Gabor patches or bars (Polat and Sagi, 1993; Polat and Sagi 1994b; Kapadia, Gilbert and Westheimer, 1995). The type of modulation, which can be either a reduction or an increase of contrast thresholds, depended on their relative

orientation and separation with respect to the target. It has been shown that the contrast threshold of Gabors presented in the fovea decreases in the presence of co-oriented and co-aligned (collinear) flankers (Polat and Sagi, 1993; Polat and Sagi 1994b; Kapadia et al., 1995; Bonneh and Sagi, 1998; Polat and Norcia, 1996). The peak of this facilitation is reached when a target-to-flanker separation is approximately three times the Gabor carrier wavelength (3λ). On the other hand, smaller separations can increase the target contrast threshold, depending on the flankers' contrast and the phase of the cosinusoidal carrier (Zenger and Sagi, 1996). Complementary to those findings, physiological data have suggested that the substrate of these spatial interactions may be found at the early level of visual processing (Polat and Norcia, 1996, Kapadia, Westheimer and Gilbert, 1999; Nelson and Frost, 1985; Knierim and Van Essen, 1992, Li and Li, 194; Mizobe, Polat, Pettet, Kasamatsu, 2001; Toth, Rao, Kim, Somers and Sur, 1996; Li, Their and Wehrhahn, 2000, 2001).

This pattern of lateral interactions between early visual cortical neurons, which results from different target-to-flankers separation distances, may be altered by practicing target contrast detection through a process referred to as perceptual learning (Polat and Sagi, 1994b; Polat et al., 2004). For instance, it has been shown that after a series of training sessions,, the strong lateral suppression that is usually observed in an abnormal patterns of connectivity, such as in the case of amblyopia, disappears and is replaced by facilitation (Polat et al., 2004). Perceptual learning has been shown to be specific for the low-level trained stimulus and for the task, which suggests modifications of neural processes at the early levels of visual processing. Nonetheless, systematic training in low-level tasks also seems to yield significant perceptual benefits to unrelated visual functions, such as visual acuity, that may share the same linear filtering at an early stage of processing (Polat et al., 2004, Tan and Fong, 2008; Polat, 2009).

To date, most investigations on the pattern of lateral interactions as well as their modulation through the process of perceptual learning and the transfer of low-level learning to high-level tasks have been conducted with stimuli presented in central

vision. When the stimulus position is off-fixation (e.g., from 1° to 4° eccentricity), results are less consistent: despite Polat and Sagi (1994b) reported in a footnote that facilitation took place at 3° of eccentricity with the "same pattern of enhancement" as for foveal vision, no specific data was reported with regards to foveal vision. However, Williams and Hess (1998) testing at 3° eccentricity, did not find facilitation for separations of 3λ. With a target–flanker separation of 6λ, one of their three subjects did show weak, but statistically significant, facilitation. Another study by Zenger, Landolt and Koch (2001) tested their participants at 4° eccentricity and a target–flanker distance of 4λ, and reported a suppression effect rather than a facilitation one. In general, there is failure in finding collinear facilitation despite the fact that the stimuli are M-scaled. At 4° eccentricity and spatial frequencies of 3-4 cpd, Shani and Sagi (2005) found facilitation that was larger when stimuli were presented with orthogonal flankers than with collinear flankers. Previous reports on the effect of flankers in peripheral vision are contradictory. One study (Giorgi, Soong, Woods and Peli, 2004) reported collinear facilitation at the periphery, but since the collinear condition was compared with a no-flankers condition (instead of an orthogonal or "cue"-condition), it is not possible to determine whether the facilitation is due to lateral interactions or to a more general spatial uncertainty reduction effect.

Furthermore, it is unclear whether perceptual learning modulates lateral interactions in the periphery. Fittingly, previous results are not consistent (Shani and Sagi, 2005), but this is possibly due to an insufficient number of sessions (Li, Provost and Levi, 2007). In Experiment 1, we attemped to provide some answers on the aforementioned inconsistencies by investigating lateral interactions in the periphery and whether or not these can be modulated by training the contrast detection of a flanked target, either by reducing the inhibitory or by strengthening the facilitatory lateral interactions between the target and flankers. Moreover, we explored whether training-dependent reduction of low-level inhibitory lateral masking could reduce the peripheral masking effect known as crowding (Levi, Hariharan and Klein, 2002; Levi, 2008; Pelli and Tillman, 2008).

Crowding occurs when there is a decrease in visual discrimination for a particular stimulus when it is presented with flanking elements (Levi et al., 2002, Chung, Levi and Legge, 2001). In fact, although inhibition of contrast detection and crowding are two distinct phenomena (Levi et al., 2002; Petrov, Popple and McKee, 2007), they may share the same first stage of linear filtering (Chung et al., 2001).

In Experiment 1, each observers's set of visual functions were examined in order to determine baseline performances. The contrast sensitivity function (CSF), visual acuity (VA), the strength of the crowding (CW) and the influence of collinear and orthogonal flankers on the contrast detection of a central and vertically oriented Gabor patch of 4 cpd (Fig. 1) were all assessed. All stimuli were placed at 4° eccentricity, randomly either to the left or to the right with respect to a central fixation point. Prior to testing, observers performed training sessions on the collinear configuration using different spatial frequencies across four target-to-flankers distances (from 2λ to 8λ), the same setup that was used in the pre-training sessions. A yes/no task and the psychophysical method of Constant Stimuli were used to estimate the contrast threshold values at which subjects perceived the target with a probability of 0.6 and 0.8. Since previous studies have shown that lateral interactions induce facilitatory modulations mainly at low contrast values (Bonneh and Sagi, 1998; Polat and Norcia, 1996; Tailby, Cubells and Metha, 2001; Adini and Sagi, 2001; Polat, Mizobe, Kasamatsu and Norcia, 1998; Polat and Sagi, 1993), this study aimed to compare the effect of learning for these two contrast thresholds.

Method

Apparatus

Stimuli were displayed on a 19-inch CTX CRT Trinitron monitor with a refresh rate of 75 Hz. The flankers and target stimuli were generated with the Matlab Psychtoolbox (Brainard, 1997; Pelli, 1997) whereas stimuli for VA and CW were generated using E-

Prime software. The screen resolution was 1280 x 1024 pixels. Each pixel subtended ~1.9 arcmin. We measured CSF by using sinusoidal gratings generated by a VSG2/3 graphics card. Gratings were displayed on a 17-inch Philips Brilliance 107P CRT monitor with a refresh rate of 70 Hz and a spatial resolution of 1024 × 768 pixels. We used a gamma-corrected lookup table (LUT) so that luminance was a linear function of the digital representation of the image.

Subjects

Eight subjects (mean age: 28.3, SD: 6.3) who were unaware of the purpose of the study participated in the experiment. Subjects sat in a dark room 57 cm from the screen. Viewing was binocular. They were instructed to fixate on a central fixation spot. All subjects had normal or corrected-to-normal visual acuity. All subjects gave their informed consent prior to their inclusion in the study. We have performed the study in accordance with the ethical standards laid down by the 1964 Declaration of Helsinki. The study was approved by the Ethics Committee of the Department of General Psychology, University of Padua. We obtained written, informed consent from all participants involved in the study.

Training stimuli

Stimuli used for the training were Gabor patches constituted by of a cosinusoidal carrier enveloped by a stationary Gaussian. Stimuli were showed on a display with mean luminance of 46.7 cd/m_2. The Equation for generating the Gabor was the following:

$$G(x, y) = \cos(2\pi / \lambda x + \varphi) \exp(-(x^2 + y^2) / \sigma^2) \qquad \text{Eq.1}$$

In which λ is the sinusoidal wavelength, φ the phase, the SD of the luminance Gaussian envelope (σ). For all the configurations, σ = λ and φ = 0. The special frequencies used were 1, 2, 4, and 8 cpd. Respect to the central fixation point (with diameter of 0.18 deg), the target was located at 4 deg either to the left or to the right. The target was a low-

contrast vertical Gabor target flanked, above and below, by two high-contrast (0.6 Michelson contrast) Gabor patches (Figs. 1A and 1B, respectively). In the training sessions, the flankers were always vertically oriented and placed at different target-to-flankers separations (i.e., 2λ, 3λ, 4λ, and 8λ). For spatial frequencies of 1, 2, and 4 cpd, target's contrast levels ranging from 0.016 to 0.1 (Michelson contrast) in steps of 0.2 log units were used, whereas for the spatial frequency at 8 cpd, the contrasts ranged from 0.023 to 0.59 (Michelson contrast) in steps of 0.35 log units. The rationale for using different range of contrast levels for the higher spatial frequency was to facilitate the detection of the stimuli. Moreover, an additional contrast level of 0.0 (Michelson contrast) was used, as "catch trials", in order to measure false alarms .

Figure 4. Stimuli used in the experiments.

(A) Collinear configuration: the target (central patch) has the same orientation as that of the flankers. (B) Orthogonal configuration: the flankers are oriented horizontally with respect to the central vertical target.

In this example, the stimuli are located to the right with respect to the fixation point (4° eccentricity), and their position was randomized across trials. The stimuli showed here have a spatial frequency of 4 cpd, and the target-to-flankers distance is 3λ. The target (central patch) has a lower contrast than the flankers. For illustrative purposes, the Gabor patches here have exaggerated contrast.

VA and CW stimuli

The stimuli were 10 randomly chosen alphabet letters (D, N, S, C, K, R, Z, H, O, V) that were each presented for a duration of 100 ms. In the VA test, the location of the target letter was 4° either to the left or the right (randomly chosen trial by trial) with respect to the fixation point. The size of the letters varied according to a 1up/3down staircase (Levitt, 1971). The step size was 0.186 arcmin (vertical font streak), , the character type was Arial, and the starting size for the letter was 3.72 arcmin. Subjects had to say the letter displayed and the experimenter registered the answer. The session terminated after either 100 trials or 8 reversals. A threshold acuity, expressed as the font size for 79% correct identifications, was the mean of the 8 reversals.

In the CW test, the target letter was flanked on the left and the right sides by two different letters. The triplets could appear randomly either to the left or to the right of the fixation point, but the target letter was always at 4 deg from the fixation spot. In the CW test, the size of both the target letter and flanking letters was set 20% bigger than the VA threshold. Inter-letter distance varied according to a 1up/3down staircase (Levitt, 1971). The initial distance between letters was set at 95 arcmin, and the step size was constant at 1.9 arcmin. The session terminated either after 100 trials or 8 reversals. At the end of the procedure, we calculated the threshold by averaging the distance values in correspondence with the 8 reversals.

CSF stimuli

We measured peripheral CSF with vertical gratings displayed on the whole screen area except for the fovea. This was carried out by placing a circular black spot (4° radius, the same eccentricity used for stimuli presentation in the training sessions) at the centre of the screen to force subjects to attend the near-periphery of their visual field while fixating on the center of the dark spot. Individual contrast thresholds were estimated with the Method of Limits over seven spatial frequencies (0.1, 0.2, 0.4, 0.9, 2.0, 4.5, and 10.2 cpd).

Procedure

Contrast sensitivity functions (CSF), visual acuity test (VA) and crowding test (CW), in addition to contrast thresholds for the lateral interaction task, with both collinear and orthogonal flankers, were measured initially to establish individual baseline performances and after the training period. We tested lateral interactions by comparing the contrast detection of a vertical Gabor target (4 cpd) flanked by either two vertically oriented Gabor patches (collinear condition – Fig. 1A) or two horizontal Gabors (orthogonal condition – Fig. 1B) with target-to-flankers distances of 2λ, 3λ, 4λ, and 8λ. The contrast detection threshold was measured for the target Gabor presented at 4 deg of eccentricity. Each stimulus was presented for 133 ms.

A standard training block consisted of a contrast-detection task on the central Gabor patch flanked by two high-contrast and collinear Gabor patches. A typical daily session consisted of four blocks, in which the target-to-flankers distance varied, starting from the highest distance (8λ). A weekly session consisted of four consecutive daily sessions. The spatial frequency of the Gabor patches varied between daily sessions, starting from the lowest spatial frequency (1 cpd). Each experimental block consisted of 96 randomly presented trials that corresponded to 8 repetitions of 12 stimulus conditions: 6 (contrast levels) x 2 (spatial positions). The Method of Constant Stimuli and a yes/no detection paradigm were used. Thus, a standard daily session comprised 384 trials separated in

four blocks, each dedicated to one target-to-flankers distance. Globally, each subject performed 160 sessions distributed over the course of 8 weeks. A logistic function was fitted to the data in order to estimate the contrast thresholds at which the subjects detected the target with a probability of 0.6 and 0.8.

For all the comparisons, we used Student's t-tests.

Results

Lateral masking curves

Fig. 5 shows the lateral masking curves that we derived from the pre-test contrast thresholds associated to either 0.6 (low contrast threshold - LT) or 0.8 (high contrast threshold - HT) detection probability versus target-to-flanker distances. Each contrast threshold was normalized by the baseline threshold for the orthogonally flanked target at a separation of 8λ. Lateral masking curves differ from those in the fovea in several aspects (Polat and Sagi, 1994a, 1994b; Shani and Sagi, 2005) ; that is, at 4λ (a distance that produces consistent facilitation in the fovea), we did not find facilitation, which is in agreement with other studies (Zenger-Landolt and Koch, 2001). Moreover, it should be noted that target-to-flankers separations of 3λ lead to inhibition instead of facilitation, as previously found (Shani and Sagi, 2005). This result is in contrast with a brief comment in Polat and Sagi (1994b) in which authors claimed collinear facilitation in the near-periphery at the same target-to-flankers separation. However, no data in support of that statement were reported by the authors. The new result is that normalized LT reveal a collinear facilitation at a target-flanker distance of 8λ (t_7=-2.91, p=0.023). The lateral masking curve referring to normalized HTs had a similar trend as

the curve associated with LTs; however, in this case, we did not find any facilitation at 8λ (t_7=-1.33, p=0.22).

Target suppression was found at a target-to-flanker distance that produces facilitation in the fovea (≈3λ), and this is compatible with the physiological finding that surround suppression increases with eccentricity (Petrov et al., 2007). On the other hand, we found a consistent collinear facilitation for LT at separations of 8λ. This pattern suggests the presence of facilitatory lateral connections with larger extent in the near periphery respect to the fovea, consistently with the most recent studies on peripheral lateral interactions (Lev and Polat, 2011) . The interpretation of this effect is not straightforward, because cell recordings showed that, in macaque area V1 at 2° – 8° eccentricity, horizontal connections in layers II/III extend only 6±0.7 mm on average (Angelucci and Bullier, 2003), whereas a human's V1 columns are only about twice the size of a macaque's V1 columns (Cheng, Waggoner and Tanaka, 2001). One possibility is that facilitation at such large separations is mediated by a cascade of long-range interactions (Polat and Sagi, 1994b). Moreover, we only found facilitation at 8λ for the low contrast threshold, not for the high contrast threshold. This is consistent with the physiological finding that neuronal facilitation preferentially occurs when the collinearly flanked target is near its detection threshold (Bonneh and Sagi, 1998; Polat and Norcia, 1996; Zenger-Landolt and Koch, 2001; Tailby et al., 2001; Adini and Sagi, 2001; Polat et al., 1998).

Moreover, it is interesting to note that Giorgi et al. (2004) reported that the important difference between Polat and Sagi (1994b) who reported facilitation (but it is worth to note, did not report data whatshoever) and later studies that did not (Williams and Hess, 1998; Zenger-Landolt and Koch, 2001) was the technique used to test subjects: temporal two-alternative forced choice (2AFC) vs spatial-2AFC. In Experiment 1, we used a yes/no procedure and yet we found facilitation. So, at least partially, this effect seems independent from the technique by which is measured.

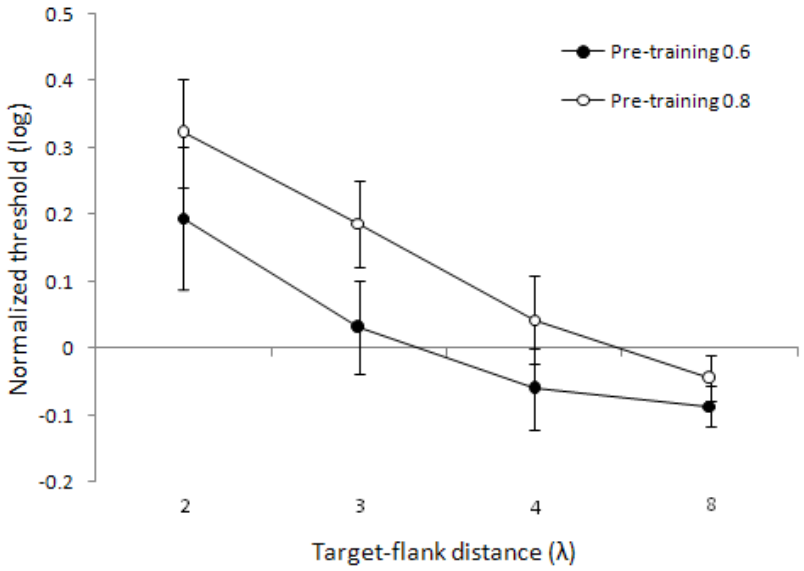

Figure 5. Detection thresholds for 0.6 and 0.8 probability levels.

Thresholds corresponding to 0.6 probabilities (filled circles) and 0.8 probabilities (open circles), normalized by orthogonal flankers at 8λ as a function of the target-to-flanker distances (λ). Error bars ± 1 s.e.m.

Perceptual learning

Training the contrast detection of a collinearly flanked target resulted in a significant decrease of contrast thresholds, but the learning effect did not transfer to the target of the same orientation and orthogonally oriented flankers (Fig. 6) Threshold reduction after training becomes more consistent as the target-to-flankers separation decreases in the range of 4λ - 2λ. Especially in the case of LT, the threshold significantly decreased at 3λ (t_7=3.30, p=0.013), whereas for the other target-to-flankers distances, we did not obtain any significant difference between the contrast thresholds measured in the pre and post-training sessions. In the case of HT, thresholds significantly decreased at 2λ (t_7=3.38, p=0.012) and at 3λ (t_7=3.48, p=0.010). At 8λ, where collinear flankers

facilitate the observer's detection of the low-contrast target, training had no effect on either LT or HT. These results support the evidence that learning only reduces the suppression of the flankers (Polat et al., 2004).

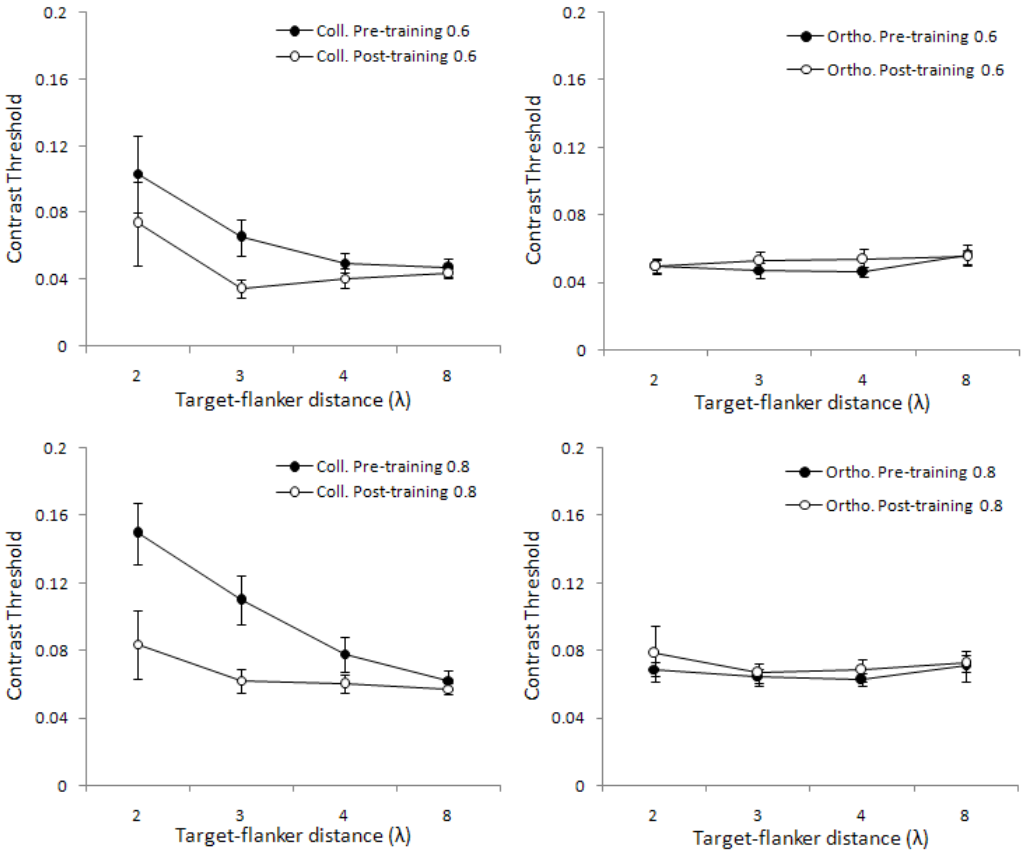

Figure 6. Contrast thresholds for target flanked by collinear and orthogonal flankers, before (pre) and after (post) training.

Mean detection thresholds corresponding to 0.6 (top row) and 0.8 probabilities (bottom row), as a function of the target-to-flanker distances (λ), for the target flanked by collinear flankers (left column) or orthogonal flankers (right column). Data refer to Gabors with a spatial frequency of 4 cpd. Filled circles

refer to pre-training measurements, and open circles refer to post-training measurements. Error bars ± 1 s.e.m.

Since the yes/no procedure that we have used is sensitive to response bias (Wenger, Copeland, Bittner and Thomas; 2008), the procedure may have had a significant impact on the reported thresholds. To check for this possibility, we have reanalyzed the data by calculating *d'*, which is a measure of sensitivity that is independent of bias. We calculated *d's* according to the Signal Detection Theory by using the accuracy data obtained in the catch trials (0.0 Michelson contrast) and in the second highest contrast condition at all target-to-flankers separations. The results appear in Fig. 7. The *d'* results reflect results obtained by measuring thresholds: sensitivity decreases progressively as λ decreases, and the effect of learning is only significant at 2λ (t_7=-2.64, p=0.034) and nearly significant at 3λ (t_7=-2.11, p=0.073); at 4λ and 8λ, where sensitivity is very high, there is no significant learning effect (t_7=-1.57, p=0.16 and t_7=-0.75, p=0.48, respectively).

Furthermore, the proportion of false alarms did not depend on whether the observer received training on any target-to-flanker distance (2λ: t_7=0.02, p=0.98; 3λ: t_7=0.16, p=0.87; 4λ: t_7=0.068, p=0.95; 8λ: t_7=1.02, p=0.34).

Perceptual learning improves visual performance in human adults, specifically for the trained task, pointing to plasticity in the adult visual cortex during training (Cheng et al., 2001). Several studies indicate a plasticity of lateral interactions that results from repetitive practice on detecting a flanked-target. The increased range of facilitatory interactions between target and flankers most likely reflects the effect of training (Polat et al., 2004) that produces a reduction in strength of short-range suppressive interactions between target and flankers (Zenger and Sagi, 1996). We showed that perceptual learning with stimuli presented in the near periphery reduced short-range inhibition at 2λ and 3λ, but it did not increase facilitation. This is a new result: in fact previous

studies, such as the one of Shani and Sagi (2005)conducted with similar eccentricity, separations and spatial frequencies as those used in the present study did not find a consistent effect of training. This discrepancy may be due to the fact that we employed an appropriate number of sessions (Li et al., 2007).

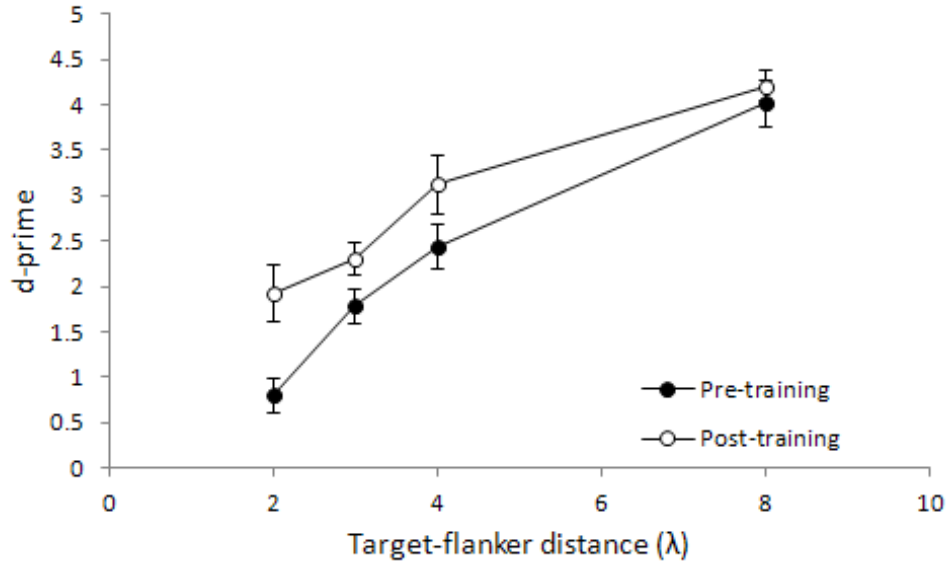

Figure 7. Detection sensitivity for target flanked by collinear flankers, before (pre) and after (post) training.

Mean d-prime as a function of the target-to-flanker distances (λ) for the target flanked by collinear flankers. Data refer to Gabors with a spatial frequency of 4 cpd. Filled circles refer to pre-training measurements, and open circles refer to post-training measurements. Error bars ± 1 s.e.m.

Transfer of learning to orthogonally flanked Gabors

The high stimulus specificity observed in the learning studies (Polat et al., 2004; Gilbert, Sigman and Crist, 2001) points to an activity-dependent plasticity of the visual cortex, in which the specific interactions activated during training are modified to

improve performance. We also confirmed the specificity of lateral interactions modulation, because we found an absence of a learning effect for the orthogonally flanked target that has the same orientation as the trained target. The lack of transfer of learning to a stimulus with the target having the same orientation but with flankers of different orientation suggests that perceptual learning affects not only the response of the individual underlying filter (Bao, Yang, Rios, He and Engel, 2010) but also its contextual modulation by co-axial filters outside its receptive field (Kapadia et al., 1995).

Transfer of learning to CSF

In recent years, a number of studies produced evidence for the connection between lateral interactions and contrast response (Bonneh and Sagi, 1999; Cass and Alais, 2006; Cass and Spehar, 2005; Ellenbogen, Polat, and Spitzer, 2006; Polat and Norcia, 1996; Polat and Sagi, 1993, 1994a, 1994b, 2006; Shani and Sagi, 2006; Solomon and Morgan, 2000; Tanaka and Sagi, 1998; Woods, Nugent, and Peli, 2002) supporting the idea that early stages of visual analysis play an important role in generating this effect.. Polat (2009) proposed that CS is a fundamental function that reflects the output of early visual processing. More specifically, author stated that it represents the performance of the neurons at the primary visual cortex. Improvement in CS may facilitate the performance of visual processing during the next stages of the visual cascade, which rely on the output of these neurons.

Contrast sensitivity in the near-periphery was measured with standard methods before and after training in order to derive CSF for sinusoidal gratings at a range of spatial frequencies. Training lateral interactions increased contrast sensitivity only at the highest spatial frequency used (10.2 cpd) (t_7=-4.21, p=0.004) (Fig. 8). It should be noted that the sensitivity for this spatial frequency is normally very low, at 4 deg of eccentricity.

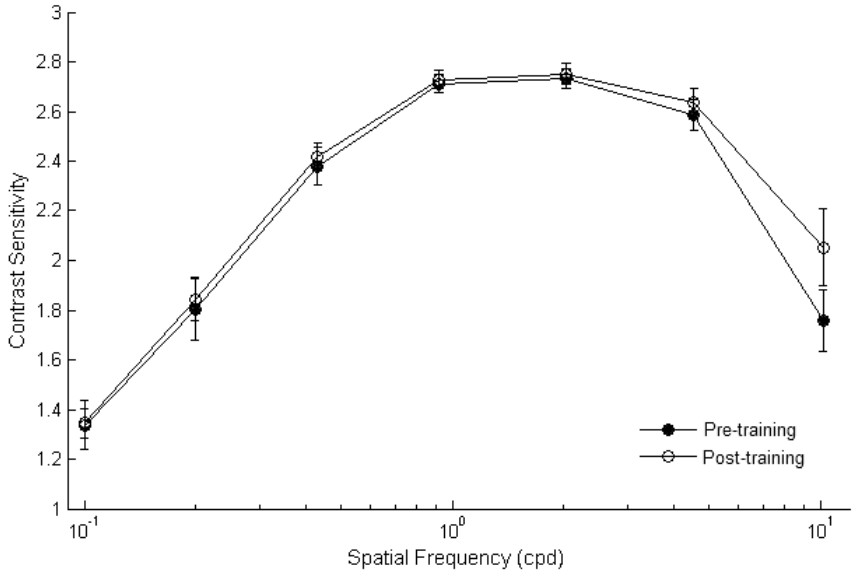

Figure 8. Contrast Sensitivity Functions, pre and post-training.

Mean CSFs measured before training (filled circles) and after training (open circles). Sensitivity improved by a factor of ≈0.5 at the highest spatial frequency (10.2 cpd). CSFs were tested by using sine-wave gratings that varied in contrast and excluded the fovea (± 4°). Error bars ± 1 s.e.m.

Transfer of learning to VA

Any incoming visual information is sampled by spatial filters in the visual cortex, and each filter is selective for a narrow range of spatial frequencies, the weak response of filters tuned for high spatial frequencies in the periphery is expected to limit VA. Thus, an improvement of the sensitivity for high spatial frequencies after the training period should improve peripheral VA. However, results (Fig. 9) showed that the reduction of suppressive lateral interactions after training did not improve VA in the peripheral

visual field (t_7=0.424, p=0.685). A possible explanation to this result is that we trained only one orientation and we measured VA using alphabetic letters as stimuli that are made up of line segments with different orientations. It is possible that training had not generalized to every spatial orientation and therefore was not able to improve the observers' VA. Another possibility is that learning did not transfer to letter acuity because letter acuity depends on accurate encoding of a relative phase in addition to sensitivity to contrast, spatial frequency and orientation.

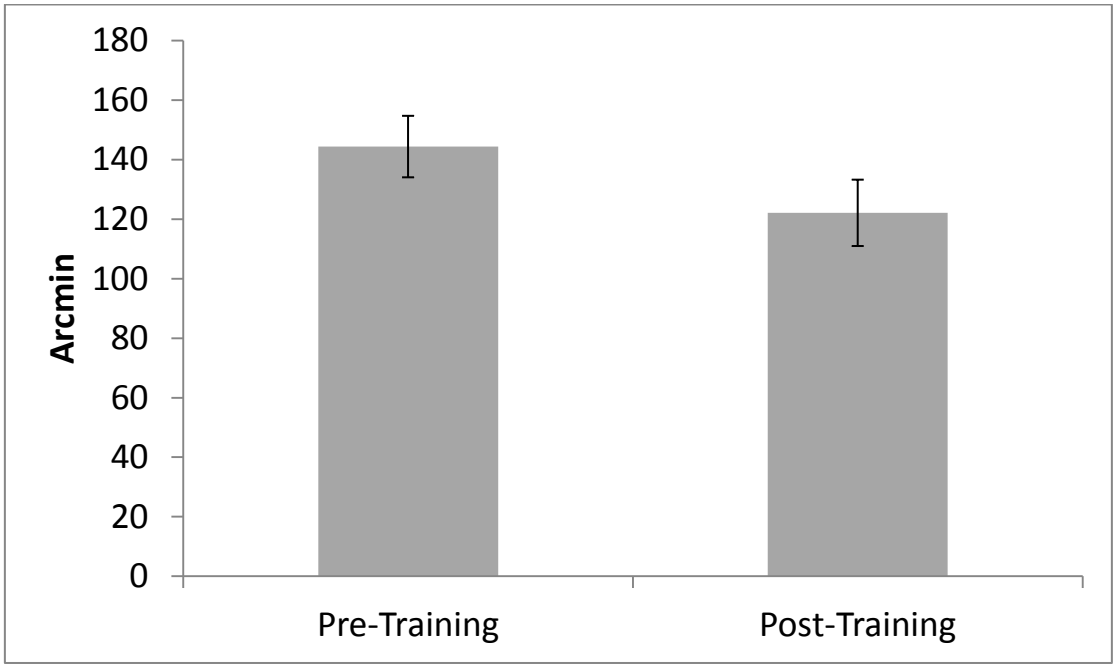

Figure 9. VA before and after training.

Mean VA, expressed as the arcmin dimension that allowed 79% of correct identification of the letter presented at 4 deg of eccentricity. Error bars ± 1 s.e.m.

Transfer of learning to CW

Although training-dependent reduction of lateral suppression caused by collinear flankers at 2λ and 3λ had no effect on VA, it significantly reduced crowding in

peripheral vision (t_7=3.59, p=0.009) so that the observer could better identify a target in a cluttered background (Fig. 10).

The dissociated effect of training on VA and CW may be a consequence of the fact that the strong lateral masking in the periphery is more likely to degrade identification when the target letter is surrounded by other letters rather than when the target letter is presented in isolation (Levi, 2008). This masking phenomenon, known as crowding, increases with the eccentricity of the target, but it is relatively independent of the target's size (Levi, 2008). Although many studies have claimed that CW reflects the combination of inappropriate features, the similar properties of surround suppression and crowding suggest that surround suppression may, at least in part, explain CW. Based on this assumption, it is not unlikely that the reduction of inhibitory lateral interactions has more effect on an observer's ability to identify crowded letters than on the observer's ability to identify single letters. Crowding is a peripheral phenomenon, so we do not expect it to be present in the fovea. However, letters to be identified are surrounded by other letters in the standard VA tests (ETDRS), so there is also the possibility that in previous studies, the effects of CW have been confounded with those of VA (for a review, see Levi, 2008). We did control for this confounding by measuring VA with only the letter-size as the dependent variable. Thus, we were able to dissociate the training's effect on VA from its effect on CW.

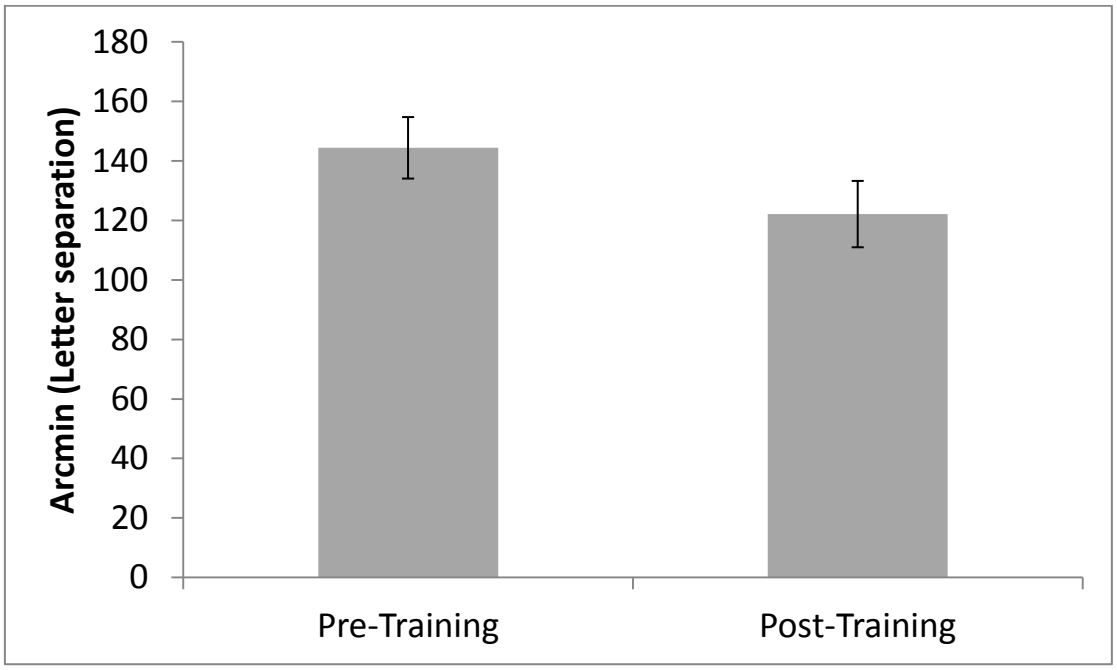

Figure 10. Results for the crowding (CW) test

CW is expressed as the distance (arcmin) between the target and the flankers letters. The target and flankers' font size corresponded to the font size threshold estimated in the VA task and increased by 20%. Error bars ± 1 s.e.m

Discussion

The first interesting result of Experiment 1 is the presence of consistent collinear facilitation at the periphery of the visual field. This result is consistent with the most recent investigation, to date, on peripheral collinear facilitation (Lev and Polat, 2001), that reported facilitation for a target-to-flankers separation of 7λ.

A previous study by Giorgi et al (2004) claimed to have found collinear facilitation in the periphery, but since they did not distinguish between actual lateral interaction effects (orientation and spatial frequency-sensitive) and spatial uncertainty reduction, by comparing collinear with no-flankers condition, our study is the first to show the presence of facilitatory, collinear lateral interactions in the visual field.

Moreover, it is worth noting that Shani and Sagi (2005) also reported that some subjects exhibited facilitatory lateral interactions without the manipulation of attention in the task. Our results suggest the presence of different lateral-interactions in the periphery with respect to the fovea. Facilitation was found at larger separations than those at which the flankers affected the observers' detection of foveal targets whereas suppressive interactions occurred at a larger range of target-to-flankers distances than in the fovea. Moreover, it was found that training lateral interactions at different ranges of target-to-flankers distances reduced suppression but did not increase facilitation. Most importantly, results indicated that learning did reduce CW in addition to improving contrast sensitivity for high spatial frequencies, whereas it had no effect on VA.

The finding that facilitation of target detection by the flankers occurs at larger separations in the periphery seems to be incompatible with the finding of Angelucci and Bullier (2003), who demonstrated that long-range connections in layers II/III of the macaques' striate cortex at 2° – 8° eccentricity extend about 6±0.7 mm, whereas human striate cortex columns are about twice the size of the macaques' V1 columns (Chung et al., 2001). Thus, it is possible that the larger extent of facilitatory lateral connections in the near periphery could be mediated by a concatenation of long-range interactions, as suggested by Polat and Sagi (1994b).

In contrast to a previous study by Shani and Sagi, (2005) we found that inhibitory long-range interactions were reduced by the training whereas their results seem more inconsistent since the reduced inhibition brought about by training was only exhibited in one subject. This inconsistency probably arose from the study's insufficient number of training sessions (Li et al., 2007) which highlights the importance of practice and

continuity in order to enhance neural plasticity. Thus, by training subjects for 8 weeks (about 50 hours), the present study found a significant effect on the trained collinear flankers condition but no effect on the untrained orthogonal flankers condition. This last result is consistent with the selective effect of training on reducing suppressive lateral interactions. In previous studies, perceptual learning has been shown to be specific for the low-level trained stimulus and for the task (Gilbert et al., 2001; Bao et al., 2010; Sagi and Tanne, 1994), which suggest that modifications of neural processes at the primary visual cortex takes place in adults. Perceptual learning has also been shown to be specific for collinear flankers. However, our results showed that systematic training in this low-level task yielded significant perceptual benefits to unrelated visual functions (e.g., crowding) and this is in agreement with other findings (Polat et al., 2004; Polat, 2009; Tan and Fong, 2008). How can the reduction of the strength of inhibitory low-level lateral-interactions explain the reduced crowding effect? One answer may be found in the study by Pelli and colleagues (2004), who argued that crowding reflects an excessive feature integration process, so it is possible that the reduction in strength of the inhibitory long-range lateral-interactions at the low-level may determine a more appropriate balance between inhibition and integration processes. Crowding for letters is likely to occur at the level of area V4, since it has been shown that macaques' receptive fields in V4 have an extension of about 0.5 ϕ (where ϕ represents the target eccentricity), which fits well with the extent of peripheral crowding for letters (Motter, 2002). Coherent with these findings, our study may explain that the effect of the training on letter crowding may reflect the weakening of inhibitory long-range connections present at the level of area V1. However, it is not clear how reduced inhibition at low-levels can modulate the integration processes at higher levels. Cell recordings pointed out the existence of direct projections from V1 to V4 bypassing V2 (Nakamura, Gattass, Desimone and Ungerleider, 1993). It may be possible that the weakening of inhibitory long-range interactions after training the low-levels, might be forwarded to area V4 by exploiting secondary routes from V1. Although the inhibition

of contrast detection by flankers and crowding are two distinct phenomena (Levi et al., 2008; Petrov et al., 2007), they may share the same primary stage in which linear filtering processes take place. However, since crowding is a phenomenon that takes place with suprathreshold stimuli (Levi, 2008), this hypothesis may be questionable. Alternatively, instead of or in addition to feature learning, it is possible that the lateral masking stimulus induceseither location-learning (Xiao, Zhang, Wang, Klein, Levi, et al. (2008)) or rule-based learning (Zhang, Zhang, Xiao, Klein, Levi et al. ,2010) in a central site, which in turn increases an efficient modulation of low and high-level inhibitory processes. More specifically, it is possible that learning occurs in a central site and consists of a reduction of inhibitory effects through external noise exclusion (Lu and Dosher, 1998), both at a low and high level of processing. Indeed, the variation of spatial frequencies and target-flankers separation during practice may have produced conditions that maximized the amount of transfer to new tasks. However, the lack of transfer to orthogonal condition challenged this interpretation.

In any case, previous studies using perceptual learning on tasks involving low-level visual functions (Polat et al., 2004; Tan and Fong, 2008, Polat, 2009) showed that the improvement in contrast detection transferred to higher level visual functions. It has been suggested by the authors that these higher level abilities are indeed built on low level functions in a hierarchical organization. In conclusion, the present study has shown that probing cortical interactions with a wide range of spatial frequencies and target-to-flankers separations could possibly modulate the spatial interactions in the peripheral visual field of normal sighted human adults. Most importantly, reduced lateral masking through perceptual learning in the periphery reduces crowding and consequently increases acuity for the target stimulus. Crowding is ubiquitous in spatial vision and occurs in a variety of tasks, including letter identification (Bouma, 1970; Flom, Weymouth and Kahneman, 1963; Toet and Levi, 1992), vernier acuity (Westheimer and Hauske, 1975; Levi, Klein and Aitsebaomo, 1985), stereoacuity (Butler and Westheimer, 1978), and orientation discrimination (Westheimer,

Shimamura and McKee, 1976). Therefore by reducing crowding, perceptual learning may allow the periphery to perform several tasks in viewing conditions that are more similar to those present in central vision. This has important implications for the rehabilitation of low-vision patients who have lost the use of the fovea through macular degeneration, since in order to be able to perform tasks which normal sighted subjects perform in the fovea, these patients must exploit and optimise their peripheral vision.

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Chapter 4

Experiment 2: Specificity of the training on peripheral lateral interactions

In Experiment 1, we showed that perceptual learning on a contrast detection task performed in the near-periphery of the visual field (4° of eccentricity) is effective in reducing contrast thresholds when subjects were trained with a lateral interactions paradigm. Most importantly, we reported that perceptual learning was effective in reducing crowding, a higher-level, unrelated visual function respect to the training task (contrast detection task). We concluded that the lateral masking training, probing horizontal interactions between neighbouring units codifying visual input with similar features, was responsible for this transfer of learning, consistently with previous evidence from studies conducted with foveal presentation of the stimuli (Polat and Sagi, 1994b, Polat et al., 2004; Polat, 2009). Indeed, Polat and Sagi (1994b) reported the evidence that training with a limited set of stimuli (lateral masking configurations with stimuli located at different separations) is effective in improving the interactions between distant units via a cascade of lateral connections. Moreover, Polat et al. (2004) and Polat (2009) showed how a training on a lateral masking configuration is effective in producing improvement in other not directly trained visual abilities, considered to be processed at higher-level respect to the training task.

In Experiment 2, we aimed at verifying the level at which the neural modifications induced by learning took place and whether it is the modulation of lateral interactions via perceptual learning that is responsible for the transfer effects on crowding reduction reported in Experiment 1. In order to verify this assumption and to better test the

specificity of the training, we had a new group of subjects undergoing to a contrast detection task with a lateral masking configuration (similar to the one used in Experiment 1), testing different spatial positions, local and global orientations. Since in Experiment 1 the Contrast Sensitivity Function was measured only at the same orientation (vertical) as the training configuration, we don't know whether learning transfers at different orientations.

As discussed in Chapter 2, the characteristics of learning can provide information about the stages of visual processing at which it takes place: a high level of specificity would indicate the involvement of early visual areas (such as V1); on the other hand, if the improvement in contrast detection found in Experiment 1 transfers to different spatial position, then the involvement of lateral interactions at the early stages of visual analysis would be questionable.

The specificity of the learning is considered the principal indication for the level of processing at which learning takes place. Usually, the first, low-level stage of processing is believed to compute in parallel the visual input, analyzing simple features such as orientation and spatial position (Karni and Sagi, 1991, 1993). For example, location specificity is an important indicator in localizing the stage at which learning is effective, since the receptive fields' size of the units along the path of visual analysis progressively increase (Gross and Mishkin, 1977).

The new group of subjects was trained for one week on a daily basis, with pre-test conducted on 4 different stimuli configuration (Figure 8), while the training, as in Experiment 1, was conducted only on the collinear, vertical configuration (Figure 8a)

Subjects were trained with only one target-to-flankers distance (3 λ).

We chose 3 λ as the training distance because in Experiment 1 we showed that training was able to reduce inhibition at short range of target-to-flankers separation, rather than increasing facilitation for larger distances, so we wanted to maximize the effect of training by choosing the best-fitting parameters.

Method

Apparatus

Stimuli were displayed on a 19-inch CTX CRT Trinitron monitor with a refresh rate of 75 Hz. The flankers and target stimuli were generated with the Matlab Psychtoolbox (Pelli, 1997; Brainard, 1997),.The screen resolution was 1280 x 1024 pixels. Each pixel subtended ~1.9 arcmin. We used a gamma-corrected lookup table (LUT) so that luminance was a linear function of the digital representation of the image.

Subjects

Four naïve subjects (mean age = 24.75, SD =0,96) who were unaware of the purpose of the study participated in the experiments. Subjects sat in a dark room 57 cm from the screen. Viewing was binocular. They were instructed to fixate on a central fixation spot. All subjects had normal or corrected-to-normal visual acuity. All subjects gave their informed consent prior to their inclusion in the study. We have performed the study in accordance with the ethical standards laid down by the 1964 Declaration of Helsinki. The study was approved by the Ethics Committee of the Department of General Psychology, University of Padua. We obtained written, informed consent from all participants involved in the study.

Flanker and target stimuli

As for Experiment 1, stimuli were Gabor patches consisting of a cosinusoidal carrier enveloped by a stationary Gaussian. The mean luminance of the display was 46.7 cd/m_2. Each Gabor patch was characterized by its sinusoidal wavelength λ, phase φ, and SD of the luminance Gaussian envelope (σ) in the (x, y) space of the image:

$$G(x, y) = \cos(2\pi / \lambda x + \varphi) \exp(-(x^2 + y^2) / \sigma^2) \quad \text{Eq.1}$$

In all experiments, $\sigma = \lambda$ and $\varphi = 0$ (even symmetric). Gabors had a spatial frequency of 4 cpd. The location of the target relative to the fixation point (0.18 deg) changed according to the different configurations: for the trained configuration (Figure 8a), and for the control condition with different local and global orientation (Figure 8b and 8d) the target Gabor was randomly placed either in the upper-right quadrant or in the lower-left quadrant at 5.65 deg diagonally respect to the fixation point, while for the condition with different retinal position, the target Gabor was randomly placed either in the upper-right quadrant or in the lower-left quadrant at 5.65 deg diagonally from the fixation point. A vertical Gabor target (Figs. 8) was presented flanked, above and below, by two high-contrast Gabor patches (0.6 Michelson contrast). During the training sessions, the flankers were always vertically oriented and located at a constant distance of 3λ from the target.

Contrast level were in the range of 0.016 to 0.1 (Michelson contrast) in steps of 0.2 log units,. Moreover, as in Experiment 1, we used an additional contrast level of 0.0 (Michelson contrast) in order to introduce "catch trials" to estimate the false alarms rate.

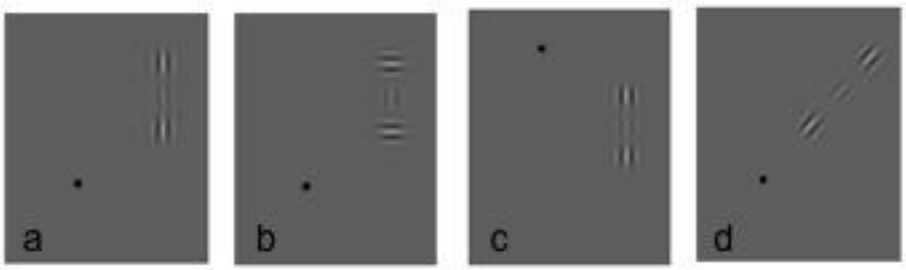

Figure 11. Stimuli used in the experiments.

(a) Collinear configuration: the target (central patch) has the same orientation as that of the flankers; (b) Orthogonal configuration: the flankers are oriented horizontally with respect to the central vertical target; (c) different retinal position: the configuration is presented in a different retinal position (lower-right), (d) different global orientation: the configuration is presented in the same retinal position but with local and global different orientation (i.e. 45°). Target-to-flankers distance was 3λ

Procedure

Contrast thresholds for the four conditions (collinear, orthogonal, different spatial location and different orientation), were measured initially to establish individual baseline performances, and retested after the training period. Target-to-flankers distance was always kept at 3λ. All the four configuration were tested at 4 deg of eccentricity. Each stimulus was presented for 133 ms. Training was carried on for one week, with daily sessions (for a total of 6 days). A standard training block consisted of a contrast-detection task on the central Gabor patch flanked by two high-contrast and collinear Gabor patches. Each experimental block consisted of 96 randomly presented trials that corresponded to 8 repetitions of 12 stimulus conditions: 6 (contrast levels) x 2 (spatial positions). The Method of Constant Stimuli and a yes/no detection paradigm were used. A logistic function was fitted to the data in order to estimate the contrast thresholds at which the subjects detected the target with a probability of 0.8. For all the comparisons, we used Student's t-tests.

Results

Learning was effective in reducing contrast thresholds for the trained configuration. We found a significant learning effect (t_3=3.44, p=0.04) obtained with the stimulus

configuration, as presented randomly in the upper-left or lower-right quadrant. For the other configurations tested, we did not find thresholds reduction neither for stimuli presented in a symmetrical retinal location (upper-right or lower-left, randomly) (t_3=-0.40, p=0.71), nor for collinear stimuli presented in the same retinal position as the learning stimulus with 45 deg orientation (t_3=-0.18, p=0.87) , nor for stimuli presented with orthogonal flankers (t_3=1.512, p=0.228) (see Fig. 12).

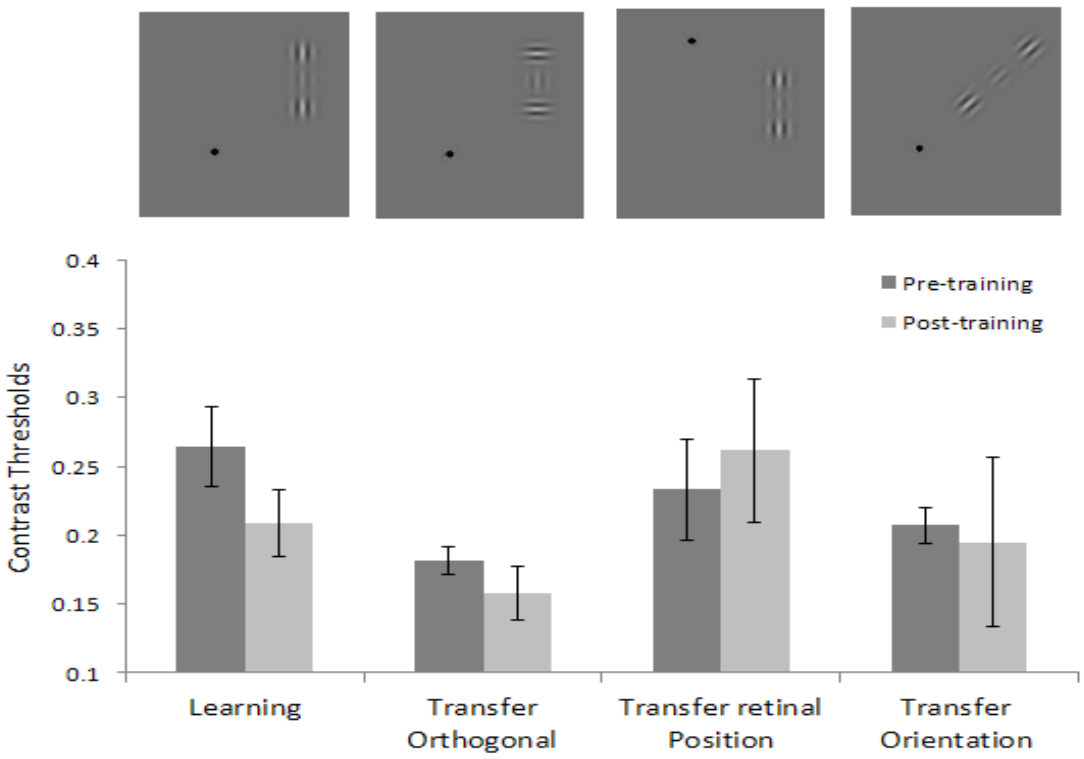

Figure 12. Specificity of learning: contrast thresholds.

Contrast thresholds for pre and post tests measurements: collinear flankers, trained, condition (column 1 and 2); orthogonal flankers condition (column 3 and 4); condition with stimuli presented in a different retinal position (column 5 and 6); condition with stimuli presented with different orientation (column 7

and 8). Gabor stimuli had spatial frequency of 4 cpd and the target-to-flankers distance was kept constant during both training and pre/post tests at 3 λ.

As for Experiment 1, in order to avoid a response bias due to the yes/no procedure (Wenger et al., 2008), we calculated *d'*, according to the Signal Detection Theory, choosing as False Alarms the accuracy in the catch trials (absence of target) and as Hits the accuracy with the highest contrast. Results are reported in figure 13.

Detection Theory by using the accuracy data obtained in the catch trials (0.0 Michelson contrast) and in the contrast level closer to the subjects' thresholds (corresponding to 60% of correct detection). The results appear in Fig. 4. As for Experiment 1, *d'* results are consistent with results obtained by measuring thresholds: Collinear configuration: t_3=3.139, p=0.05; orthogonal configuration: t_3= .049, p=0.964, different orientation: t_3=0.587, p=0.598; different spatial position: t_3=0.641, p=0.567

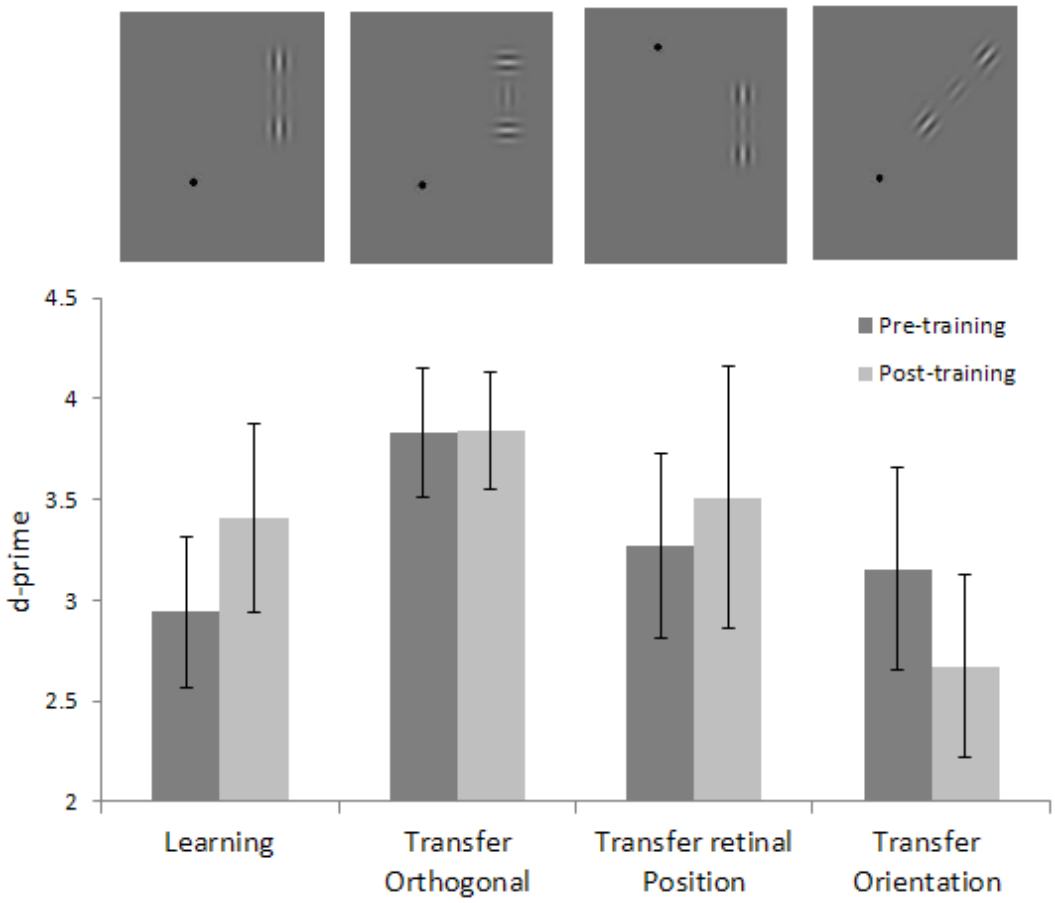

Figure 13. Specificity of learning: d prime.

d-prime for pre and post tests measurements: collinear flankers, trained, condition (column 1 and 2); orthogonal flankers condition (column 3 and 4); condition with stimuli presented in a different retinal position (column 5 and 6); condition with stimuli presented with different orientation (column 7 and 8) Gabor stimuli had spatial frequency of 4 cpd and the target-to-flankers distance was kept constant during both training and pre/post tests at 3 λ.

Discussion

As in Experiment 1, the training on lateral masking configuration at the periphery proven to be effective in reducing the contrast thresholds (and increasing the detection sensitivity) for the trained configuration, once again disproving the results of Shani and Sagi (2005) but it did not transfer to different retinal position or different local and global configurations.

Since the specificity of learning is and indicator of the stage at which learning takes place (Karni and Sagi, 1991, 1993), the absence of transfer to stimuli presenting a different orientation or spatial position suggest the involvement of the early visual areas, involved in the first stages of visual processes, further suggesting that the training conducted in Experiment 1 and 2 is able to probe lateral interactions in the primary visual cortex. This finding is consistent with experimental evidence as the one reported by Ts'o and collaborators (Ts'o, Gilbert, Wiesel; 1986) , who studied the horizontal connections and the functional structure of area V1: electrophysiological recording showed that the connections take place only between units that have the same functional selectivity. Moreover, Polat and Sagi (1993) showed how the contrast modulation due to stimuli located outside the receptive field of a given neuron is effective only when the difference in relative orientation between flankers and target is less that 45°, further pointing out the involvement of specific interactions rather then a general improvement in performance. It is worth noting that, as for Experiment 1, also in this case the contrast thresholds (Figure 12) and the d prime results (Figure 13) are quite consistent, indicating that the reduction in thresholds reported for the trained configurations and the absence of transfer for the other configurations tested in pre and post tests are due to a real improvement in performance and not in a change in strategy. The yes/no procedure seems to produce reliable thresholds, whereas previous studies on peripheral lateral interactions (Shani and Sagi, 2005; Giorgi, Soong, Woods and Peli, 2004) adopted a

spatial or temporal 2AFC. So, as for Experiment 1, peripheral lateral interactions effects seem to be at least partially independent from the method used.

Moreover, the results of Experiment 2 confirm that the improvement in higher-level visual functions reported in Experiment 1 the reduction of crowding) is the product of localized, low-level strengthening of horizontal connections, that may share some basic features with the higher level functions, so that improvement in lower level interactions can transfer a similar enhancement in performance to higher level. This is also consistent with a recent study by Lev and Polat (2011), in which authors, founding that collinear facilitation in the periphery is present at larger target-to-flankers separations, and consequently appearing related to the eccentricity, as it is for crowding, propose that both crowding and lateral masking may rely on the same lateral interactions. The idea that training can strengthen the neuronal network and improve connections between distant units via a cascade of lateral interactions has been proposed by Polat and Sagi (1994b), showing that training expanded the range of modulation. However, while testing whether the expansion of the modulatory range of lateral interactions reported in their first experiments could have been obtained by just training the larger target-to-flankers separations, Polat and Sagi (1994b) showed that training on limited separation does not produce thresholds reductions. Moreover, authors found that training on just one target-to-flankers separation produced an increase in contrast thresholds (that restored after a new, wider range-training).

According to their findings, selective training for only one target-to-flankers separation would have worsen the performance for that separation.

The reason for this difference respect to our results could be due to the extensive training (6 consecutive days; Li, Provost and Levi, 2007) or to the fact that peripheral lateral interactions are not "naturally" trained as in fovea (that means, in everyday life it is difficult to probe these interactions), so maybe these peripheral interactions are more influenced by training effects. In any case, the absence of transfer to other orientations, both absolute and local, and to different stimulus position allows us to conclude that this

high specificity points at the early stages of visual analysis for the training effects and, most importantly, that the improvement in crowding is due to modifications at low-level of visual analysis. This is consistent with the hypothesis of Polat and colleagues (2004), that suggested how the improved visual functions (visual acuity and contrast sensitivity) after training, in amblyopic patients, known to have abnormal (mainly inhibitory) lateral interactions (Polat et al., 1997, Levi, et al., 2002), is due to modifications at the early stages of visual processing induced by training on lateral interactions. The evidence that a contrast detection task could lead to improvement in higher visual function such as crowding, as we found in Experiment 1, is supported by Polat (2009), who reported that contrast sensitivity "is a fundamental function that reflects the output of early visual processing. More specifically, it represents the performance of the neurons at the primary visual cortex. Improvement in CS may facilitate the performance of visual processing during the next stages of the visual cascade, which rely on the output of these neurons."

As stated in Chapter 2, the high specificity reported in Experiment 2 lead us to believe that the mechanisms underlying these contrast thresholds modification are located at the early stages of visual processing, in which neurons are selective for stimuli features such as orientation and retinal position. Moreover, this allows us to conclude that the mechanisms involved in the transfer effects reported in Experiment 1 are of similar nature, so that improvement in higher-level visual abilities, such as crowding reduction, relies on the strengthening and expansion of lateral interactions, consistently with previous finding (Polat, 1994b, Polat et al., 2004, Polat, 2009)

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Wenger MJ, Copeland AM, Bittner JL, Thomas RD (2008) Evidence for criterion shifts in visual perceptual learning: Data and implications. Percept Psychophys 70: 1248–1273

Chapter 5

5.1 Clinical applications of Perceptual Learning paradigm

As reported in Chapter 1 and 2, lateral masking experiments showed that neural plasticity could induce contrast thresholds improvements (Polat and Sagi, 1994b, 1995; Polat, Ma-Naim, Belkin, Sagi, 2004) and that practice increases the range and modulates the strength of lateral interactions. Constraints for the improvement produced by learning are the orientation, since only collinear configuration led to contrast sensitivity and range of lateral interactions improvements, and the practice on different target-to-flankers distances. These studies underline the role of the context in the perceptual learning. In these studies, the training was proven to be effective in reducing suppression from the short target-to-flankers distances, showing that practice on lateral interactions decreases the strength of inhibitory short-range interactions and increases the strength of facilitatory interactions between neighboring units, that in turns promotes connectivity with remote units through a cascade of local interactions. This evidence offers a new perspective in using these perceptual learning paradigms for improving contrast sensitivity both in normal sighted subjects and in amblyopic subjects, who present abnormal? lateral interactions. In a series of studies, Polat (2008, 2009; Polat et al., 2004) developed a perceptual learning procedure that was designed to improve the abnormal lateral interactions in amblyopia by stimulating the deficitary neuronal networks within the visual system and probing their collinear interactions (Polat, 2008, 2009; Polat et al., 2004). The profile of the amblyopic deficits is usually not homogeneous among patients (Bonneh, Sagi, and Polat, 2004; Bonneh et al., 2007; Polat, 2008; Polat, Bonneh, Ma-Naim, Belkin and Sagi, 2005), so authors adjusted the procedure individually for each subject for maximize its efficacy. Their results showed

that perceptual learning can induce neural plasticity and is effective in reducing lateral inhibition of collinear neighbouring detectors in amblyopic patients, restoring the correct network of interactions that were abnormal in this visual disease. This pattern of results indicates that the directly trained task improved. Moreover, indications for transfer to visual abilities not directly trained come from Polat et al. (2004), in which amblyopic subjects showed the classical lower (respect to normal subjects) contrast sensitivity, especially for the higher frequencies, before treatment, but reported improvement in all the spatial frequencies, reaching the level of normal-sighted population. Moreover, 12 months after the treatment, contrast sensitivity improvements were not only still maintained, but they increased for the higher spatial frequencies.

The applications of the perceptual learning procedure defined by Polat et al. (2004) are not confined to amblyopia, since authors reported that, when running the treatment on non-amblyopic subjects, they benefited of visual acuity improvement. Tan and Fon (2008) applied on myopic patients a similar paradigm, founding an improvement in contrast sensitivity. The visual deficit in myopia is characterized by a reduced contrast sensitivity, in particular for the high spatial frequencies, respect to the normal-sighted population, similarly to amblyopic patients, but lateral interactions are normal. Therefore, a perceptual learning paradigm, probing lateral interactions in the early visual areas, is capable of improving contrast sensitivity even in presence of normal lateral interactions by further increasing their strength. Contrast sensitivity is strictly connected to visual acuity (letter discrimination) (Chung, Legge, and Tjan, 2002; Chung, Mansfield, and Legge, 1998; Legge, Pelli, Rubin, and Schleske, 1985; Levi, Song, and Pelli, 2007).In fact, contrast detection training improved visual acuity (measured with letter discrimination tasks) in amblyopes (Polat et al, 2004), anisometric amblyopes (Huang et al., 2008; Zhou et al., 2006), low myopic (Tan and Fong, 2008), and was even able to improve hyperacuity (or Vernier acuity; Levi and Polat, 1996; Levi, Polat, and Hu, 1997a). In general, it seems evident that improvement in contrast thresholds obtained after training transfer to visual acuity, a phenomenon that is consistent with the hypothesis of a relationship between contrast sensitivity? and letter discrimination. More specifically, Polat et al (2004) reported a mean improvement in contrast sensitivity of 0.34 log units after training collinear lateral interactions in amblyopic subjects. Moreover, this improvement was accompanied by an increase in

visual acuity of 0.25 log units (78%). Tan and Fong (2008), training low myopic patients, found an improvement in CSF of 0.32 log units and an improvement of Visual acuity of 0.21 log units (62%). Similar results were found for anisometropic amblyopes, with an improvement in contrast sensitivity of 0.35 log units, accompanied by an improvement of 0.136 log units (37.2%) for Visual Acuity. In both treatments subjects underwent to a training with different spatial frequencies, reaching similar improvements in the mean contrast sensitivity, though the patients were of different types (Polat et al., 2004: amblyopic; Tan and Fong, 2008: myopics). The improvement in Polat et al. (2004) reached its peak at 6 cpd, consistently with reading abilities (Patching and Jordan, 2005). Taken together, this evidence points in the direction of a larger improvement in visual acuity after a training with different spatial frequencies. Another interesting aspect that emerges from the study of Polat et al (2004) on amplyopic patients concerns the transfer of learning from the treated eye to the untrained eye: in their experiment, training was conducted monocularly, focusing on probing the deficitary lateral interactions of the amblyopic eye. After the training sessions, authors found improved binocular functions, showing that stereo acuity and binocular fusion benefited (Polat, 2006, 2008). The binocular improvement was reported for all the groups (anisometripic, strabismic and combined), indicating that training is effective even when only the amblyopic eye is treated. These benefits proved to be long terming, since most of the patients retained the improvement in a 12 months follow up test, consistently with previous studies on perceptual learning. Interestingly, 12 months after the treatments, improvements in contrast sensitivity were not only retained, but increased for the higher spatial frequencies, indicating that they were used, and thus trained, in the daily tasks. Thus, training lateral interactions triggered a learning process that continued even after that the treatment was terminated. Perceptual learning has also been used in the treatment of presbyopia. Presbyopia is an age-related visual impairment affecting near vision, that fades with age, probably due to a loss of elasticity of the crystalline lens. Presbyopic patients are usually in their forties, and by 50 almost everyone is affected by this pathology. Common treatment for presbyopia is reading glasses. Differently from amblyopia, in presbyopic patients the visual information that comes to the visual cortex is reduced by structural deficits of the eyes. Images having high spatial frequencies are perceived as having low contrast, even when

their physical contrast is high. As a consequence, contrast sensitivity is lower than normal-sighted subjects, like in amblyopia. This limited visual input can negatively influence the response of the visual units, that becomes slower and weaker, producing reduced letter identification and limiting reading abilities. However, unlike amblyopia, the lateral interactions in the visual cortex are normal, though reduced by visual blurring; another aspect that contribute to differentiate amblyopic and presbyopic population is related to the mean age: usually presbyopia affects older people, thus neural plasticity is thought to be less effective in producing improvement. Some studies on presbyopia focused on reading speed. As stated before, contrast sensitivity is related to visual acuity, and consequently to letter discrimination. Reading speed is limited by the visual span, defined as the number of letters that can be discriminated in parallel during a fixation (O' Regan, 1990). It has been suggested that the dimension of the visual span constraints the reading speed, and its reduction is responsible for slower reading (Legge, Mansfield and Chung, 2001). This visual span seems to increase with increasing presentation time (Legge et al., 2001). Moreover, Levi et al. (2007) reported that in central and peripheral vision and in the amblyopic eye, letter spacing (crowding of lateral masking) constitute a limit for reading speed. Moreover, Bonneh et al. (2007) showed that spatial and temporal crowding are connected. As a consequence, reading abilities can improve by increasing the time available for the system to process the visual information (in case of reading, the text). Perceptual learning applications on visual impairment questioned also whether it is possible to produce effective results in crowding reduction. Crowding can be defined as the inability to recognize objects in clutter, for example to identify a letter when it is presented with other letters (Stuart and Burian, 1962; Whitney and Levi, 2011 for a review). A related effect, visual masking, indicates the difficulty in identify or detect a stimulus when it is presented with masking stimuli at a close spatial location (Bretimeye, 1984 for a review). There is not general consensus about the relation between crowding and visual masking: some studies underline the link between these two phenomena (Bonneh et al., 2007; Livne and Sagi, 2007; Petrov and McKee, 2006; Polat and Sagi, 1993), whereas others suggest that they are distinct (Parkes, Lund, Angelucci, Solomon, and Morgan, 2001; Pelli, Palomares, and Majaj, 2004). Visual masking could be interpreted as a suppression of the target's perception. On the other hand, crowding is often considered as a hyper-integration of

both target and mask signals (Hariharan, Levi and Klein, 2005; Pelli et al., 2004), or impaired performance in identifying the target among distractors (Tripathy and Cavanagh, 2002). When a target is presented with other elements, the visual process needs time to properly build its perceptual representation. Usually, it takes around 100 ms to roughly extrapolate the information from a visual scene. The presence of a mask increases the time needed to create this representation, an effect interpreted as suppression (Breitmeyer, 1984; Breitmeyer and Ogmen, 2000; Polat and Sagi, 2006). However, if the system processes the image fast enough, it is viewed as presented without masking, so it can be properly perceived. In 2009, Polat designed a training in order to improve both spatial and temporal contrast sensitivity in presbyopic subjects by using perceptual learning. Authors aimed at probing lateral interactions both in the spatial and temporal domain, including backward masking on the target and flankers (Polat and Sagi, 2006) along with training on collinear lateral interactions (Polat and Sagi, 1994b). After the training, contrast sensitivity improved of 0.26 log units (95%), with a peak of 164% at 12 cpd. This pattern of results is similar to that of amblyopic and myopic patients (Polat, 2008; Polat et al., 2004, Tan and Fong, 2008). Moreover, in order to test his hypothesis that the improvement in visual functions is a product of more effective temporal processing, Polat (2009) tested the integration time for contrast detection varying the stimulus duration (temporal Contrast Sensitivity) Critical duration is considered the time of presentation for which contrast sensitivity reaches a percentage (80%) of its asymptotic value, and is an index of time constant for contrast sensitivity. Shorter critical duration is an index of higher sensitivity, indicating less overall effort for? detection (Polat et al, 2007). In Polat (2009), training produced a shortening of minimal duration needed for reaching maximal sensitivity, indicating that practice improves temporal contrast detection and, in turn, processing time. Moreover, the Visual Acuity improved of 0.26 and 0.22 log units for right and left eye. The average improvement was of 73%, similarly to what reported for amblyopia and low myopia (Polat, 2008; Polat et al., 2004;Tan and Fong, 2008). The striking result is that almost all the subjects involved in the training were able to read, from a distance of 40 cm, without wearing reading glasses. The studies here reported, though being still few, show that perceptual learning can be an effective treatment for improving the quality of life of people affected by a wide range of visual impairments. Contrast sensitivity, both spatial

and temporal, is related to other visual abilities so that a training in contrast detection can transfers to other visual functions not directly trained. This hypothesis is confirmed by the fact that visual acuity improves of a similar amount of contrast sensitivity, even if the type of training and patients were different (normal subjects, myopic, amblyopic, presbyopic). Moreover, Polat (2009) showed that temporal contrast sensitivity can also be improved by training, that in turns produced an improvement in reaction time and reading speed. Taken together, these results suggest that visual functions are composed of a cascade of different stages of visual analysis, and the improvement in both temporal and spatial contrast sensitivity at early stages of visual processing transfers to other visual function processed at later stages (Polat, 2009).

Although encouraging, these studies are very recent and the research for a conclusive clinical protocol for treating these visual impairments is still ongoing. Moreover, these studies focused on pathologies in which, though blurred, the central vision was still present. To date, no investigations have been conducted on pathologies affecting the central part of the visual field, such as maculopathy, a condition in which patients are forced to use the residual, peripheral view to overcome complex visual task. Few studies focused on testing perceptual learning in the periphery of the visual field (Giorgi et al, 2004; Shani and Sagi, 2005), but they were not able neither to find collinear facilitation, reporting strong inhibitory interactions in the early visual cortex computing the periphery, but most importantly, training seemed not to reduce such inhibition (Shani and Sagi, 2005). However, since in Experiment 1 we found both collinear facilitation (even though at larger target-to-flankers distance respect to the fovea) and perceptual learning modulation (reduction of inhibitory, short distance interactions), this opens new perspectives in developing and testing a perceptual learning paradigm that allows people who suffer from central vision loss to improve their peripheral visual abilities, overcoming the visual impairment and reaching a higher quality of life.

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5.2 Central vision damages and plasticity of the striate visual cortex.

Recently, neuroimaging studies have been conducted on humans with central vision impairment. These studies offered evidence for reorganization of visual processing after loss of foveal vision, such as in patients affected by macular degeneration. In these patients, there is a loss of bottom-up input to the cortical part responsible for representing the fovea. However, stimuli presented at the periphery of the visual field seem to be able to produce responses in that part of the deprived cortex that in absence of visual impairment responds only to stimuli presented to the fovea (Baker, Peli, Knouf and Kanwisher, 2005; Baker, Dilks, Peli and Kanwisher, 2008; Masuda Dumoulin, Nakadomari and Wandell , 2008). It is important to note that these studies presented visual stimuli only at the "preferred retinal locus" (PRL), that part of the peripheral retina that patients with macular degeneration spontaneously use as a new fixation point. In maculopathy patients, PRL substitutes the fovea in its functional role: it is used for the most demanding and active visual tasks (reading, face recognition, Timberlake, Peli, Essock and Augliere, 1987). One of the hypothesis, known as the "use-dependent reorganization" states that foveal cortex responds to stimuli presented at the PRL because it has become equivalent, at a functional level, to the fovea. The long-term use of the PRL as a new fixation point, with attentional focus to stimuli presented at this peripheral location induces the foveal cortex to respond to stimuli presented at the PRL (Baker et al., 2005). According to this hypothesis, the formerly foveal cortex should not respond to stimuli presented in a retinal locus different from the PRL. On the other hand, the "use-independent reorganization" hypothesis states that the formerly foveal cortex responds to peripheral stimuli because the foveal areas do not receive direct bottom-up input, while peripheral areas do; therefore, the deprived foveal cortex takes the only available input from cortex, responding to peripheral stimuli. According to this hypothesis, stimuli presented to both PRL and no-PRL should activate the formerly foveal cortex. Dilks and colleagues (2009) tested the hypothesis that the mechanisms underlying cortical reorganization are not specific for the PRL, that means that

activation of the foveal cortex occurs not only for stimuli presented at the PRL but also for presentation of visual stimuli to other peripheral location sharing a similar distance from the fovea. Using fMRI, these authors found strong activation of the formerly foveal cortex for stimuli presented either at PRL and no-PRL in two subjects with bilateral macular degeneration. This evidence is in favour of the use-indipendent hypoyhesis, suggesting that the reorganization of the striate cortex is due to passive, not use-dependent mechanisms.

It is worth to note that the "use-dependent reorganization" hypothesis is based on a long-term use of the PRL before the tests, not just focusing of attention to that retinal position during tests. Another question is whether the activation of the formerly foveal cortex during peripheral presentation only occurs when the stimuli are attended. Recent studies showed that attention improves activation in foveal cortex for maculopathy subjects (Baker et al., 2008; Masuda et al, 2008), however it is not clear if it is necessary. The evidence that reorganization of visual striate cortex is not specific for the retinal positions that subjects use as a functional substitute of the fovea are consistent with previous studies supporting the dissociation between reorganization and selection of the PRL. Reorganization of primary visual cortex (V1) has been reported in adult animals after localized retinal lesions (Kaas, Krubitzer, Chino, Langston, Polley and Blair, 1990; Heinen and Skavenski, 1991; Gilbert and Wiesel, 1992; Darian-Smith and Gilbert, 1995; Calford, Wang, Taglianetti, Waleszczyk, Burke and Dreher, 2000). In these studies, retinal damages were prevalently in the periphery, so that the animals did not need to have a PRL; however, even in these cases, reorganization took place. More specifically, deprived V1 units started responding to stimuli that in normal condition activate adjacent parts of the cortex. Moreover, the reorganization of V1 occurs also in case of patients affected by stroke with damage only at the periphery of the visual field. In these patients there is not need of having a PRL, but the deprived visual cortex responsible for representation of the upper left visual field started responding to input coming from cortex representing the lower left visual field (Dilks et al., 2007). Furthermore, Dilks et al. (2007) showed that some maculopathy patients who adopted PRL did not present evidence for large-scale reorganization. Apparently, cortical reorganization could take place without a functional substitute of the fovea. A further question is if stimuli presented at the PRL could produce stronger foveal cortex

activation than stimuli presented at the non-PRL. Despite finding some evidence in favour of this hypothesis, Dilks et al. (2009) stated that the data would be difficult to interpret since the patients are more used to attend stimuli at the PRL, and the stronger activation could just reflect differences in the distribution of attention. In general, Dilks et al. (2009) showed that in maculopathy patients, cortical reorganization for the deprived foveal cortex is not specific to the PRL, suggesting the involvement of use-independent, passive mechanisms.

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5.3 Experiment 3: Perceptual Learning on peripheral lateral interactions in maculopathy subjects

In Experiment 3, we aimed at studying a possible clinical application of the perceptual learning on lateral interactions at the periphery of the visual field, that in Experiment 1 already proven to be effective in improving low-level visual functions (such as contrast sensitivity) and to transfer to higher-level functions (crowding reduction). Recent studies with different types of visual impairments (specifically low myopia, presbyopia and amblyopia) showed that perceptual learning on lateral interactions is effective in improving higher-level visual functions, such as Visual acuity and contrast sensitivity, that were not directly trained (Polat, Ma-Naim, Belkin and Sagi, 2004; Polat, 2009; Tan and Fong, 2008). However, all these studies were conducted with stimuli presented in the fovea. This is, to date, the first attempt at applying a perceptual learning paradigm to improve peripheral visual functions in subjects with loss of central vision (such as maculopathy patients). Moreover, we modified the paradigm respect to Experiment 1 in order to improve the efficacy of the training by reducing spatial uncertainty. Instead of randomly presenting the training configuration at the left or at the right of the fixation point, the target configuration appeared always in the same spatial position, that in case of our group of experimental subjects, maculopathy patients, was the Preferential Retinal Locus (Timberlake Mainster, Peli Augliere, Essock and Arend, 1986), the new fixation point that people affected by macular degeneration spontaneously develop after the loss of central vision. Macular degeneration is a medical condition affecting the central part of the retina (macula) and resulting in the loss of the center of the visual field (central scotoma) while not affecting peripheral vision. Patients with this disease have difficulties in a number of tasks (e.g. reading, driving, near and far vision tasks) that severely affects the quality of their life. Macular degeneration is one of the main causes of visual impairment in older adults, with the incidence of this degeneration increasing with age (age-related macular degeneration, AMD); however, some forms can affect younger individuals, such as the Stargardt disease (also called juvenile macular degeneration). Macular degeneration can be due to different causes, typically

atrophy of the retinal pigment epithelial layer below the retina, which causes vision loss through loss of photoreceptors in the central part of the eye (the "dry" macular degeneration), or abnormal blood vessel growth in the choriocapillaris leading to irreversible damage (though bleeding and scarring) to the photoreceptors (the "wet" form of macular degeneration). Although for the wet form new drugs (called anti-angiogenics) have recently been found to stop the abnormal blood vessels growth and therefore improve vision, so far no treatment have been proven to be effective in improving the functionality of the fovea once it has been severely damaged. However, it has been shown that in individuals with macular degeneration, stimuli presented in a peripheral retinal location elicit responses in the deprived cortex that would normally be responsive only to stimuli presented to the fovea (Baker, Peli, Knouf and Kanwisher, 2005; Baker, Dilks, Peli and Kanwisher, 2008; Masuda, Dumoulin, Nakadomari and Wandell, 2008), an indication for the possibility of these typology of patients to partly overcome their central vision loss by sharpening their residual peripheral vision abilities. This can occur either via the formation of new cortical connections that process the visual signal (Darian-Smith and Gilbert, 1994), or the disinhibition of pre-existing long-range horizontal connections within V1 (Darian-Smith and Gilbert, 1994; Das and Gilbert, 1995; Masuda et al., 2008). In any case, these abilities in patients suffering from central scotoma after macular degeneration are due to neural reorganization (plasticity) at cortical level. Indeed, absence of input from the retina may modify the response properties of the foveal cortex that, deprived of its normal bottom-up input as a result of macular degeneration, begins responding to stimuli presented to peripheral retinal locations (Baker et al., 2005), resulting in visual performances that are even better than those of normal subjects at the same eccentricity (Casco, Campana, Grieco, Musetti and Perrone, 2003). A limitation in using the peripheral visual field for functions normally accomplished by the central visual field is due to the structural difference of these two, that results in a decrease of visual acuity and contrast sensitivity with eccentricity, and in an increase of the phenomenon of crowding, the disrupting effect of contextual elements on visual discrimination(Gurnsey, Roddy and Chanab, 2011). Part of these differences are due to structural differences in the fovea, but also cortical phenomena can contribute: as stated in Chapter 1, lateral interactions between units codifying similar features are more inhibitory in the periphery of the visual field

(Shani and Sagi, 2005; Williams and Hess, 1998). Despite these patients typically learn to use a specific part of the (spared) peripheral retina (i.e. preferred retinal locus, PRL; Timberlake et al., 1986) as a surrogate of the missing macula for foveal functions, they are worse in tasks as fixating, face recognition and reading and have a worse acuity and contrast sensitivity function (CSF) compared to normal subjects. Moreover, since plastic neural reorganization seems to occur not only at the PRL but to all peripheral locations, the functional superiority of the PRL respect other peripheral locations has recently been questioned (Dilks, Baker, Peli and Kanwisher, 2009). A possible way to increase the strength of intracortical connections in the human brain is by perceptual learning. Perceptual learning, as described in Chapter 2, consists in a practice-dependent improvement in a visual task performance that can persist for several months, and is specific for stimulus, task, eye presentation and retinal locus of stimulation. These specificity effects have been explained on the basis of neural plasticity, consisting in practice-dependent structural and long-term modifications of a number of properties of the mechanisms in the primary visual cortex activated by the learning task, such as spatial frequency and orientation selectivity (Karni and Sagi, 1991, 1993; Ahissar and Hochstein, 1993, 1996, 1997). As reported earlier, a number of studies showed how connections between visual units at the first stages of visual analysis can be modulated by practicing on lateral masking paradigm, (Polat and Sagi, 1994b, 1995). Recently, these evidence for improvement in visual abilities have been applied in clinical research, improving contrast sensitivity in people with low refractive defects vision (Tan and Fong, 2008; Polat 2009) or with impaired lateral interactions such as amblyopia (Polat et al., 2004). As reported in the previous section, amblyopia is considered the result of malfunctioning neural connections within visual area V1 (Polat, 1999). In the clinical practice, no therapy are currently provided for treating amblyopia in adult, since the visual deficit is considered irreparable after childhood, when the development of the visual system is completed. However, some studies indicate the possibility of inducing neural plasticity through perceptual learning in adults with amblyopia (Levi and Polat, 1996; Levi, Polat, and Hu, 1997b). The striking results of these studies is the transfer of learning from the trained tasks to other unrelated and untrained visual functions such as Visual Acuity (Huang, Zhou, and Lu, 2008; Polat, 2009; Polat et al., 2004; Zhou, Huang, Xu, Tao, Qiu, Li et al., 2006). Such a perceptual

learning paradigm has been also applied to other visual impairments, such as low myopia: Tan and Fong (2008) showed that the training produced an improvement in the visual acuity of young people with low myopia. Moreover, recently, Polat (2009) showed that training of lateral interactions produces in subjects with low presbyopia a substantial improvement of the spatial and temporal contrast sensitivity, leading to improved processing speed of target detection as well as reaction time. An important aspect of these studies is that the improvements in visual functions appear to be robust when measured in follow up tests, indicating that is a long-term modification within the visual cortex, consistently with previous studies of perceptual learning.

In most of these studies the stimuli were presented in the fovea. On the basis of our finding in the previous Experiments, in Experiment 3 we aimed at investigating the possibility of obtaining improvement in peripheral visual functions (as already showed in Experiment 1 and 2), with maculopathy patients. Moving from these considerations, we ask whether it is possible to train more efficiently the residual visual functions of patients with macular degeneration so that part of the peripheral visual field can perform functions normally accomplished by the central visual field.

To our knowledge, no data has been reported on the effects of perceptual learning in patients with macular degeneration. As reported earlier, all studies on the effects of perceptual learning on visual impairment have been carried out on patients with blurred central vision, not with missing central vision and spared peripheral vision: if it is possible to improve blurred vision due to very different causes (from optical causes such as in myopia and presbyopia, to physiological alterations at the level of the visual cortex such as in amblyopia), we should also be able to improve blurred vision at the periphery of the visual field (a normal condition for every subject) when central vision is missing. Similarly to what occurs when improving blurred vision in central vision, by training collinear lateral interactions in the spared periphery of patients with macular degeneration, we could be able to improve peripheral visual function such as crowding reduction, visual acuity and contrast sensitivity function. Since the training in Experiment 1 proven to be more effective in reducing the inhibition at short distance than increasing facilitation for larger separations (consistently with Polat and Sagi, 1994b, Polat et al., 2004), and considering the difficulties in fixation of our maculopathy patients, we decided to use a shorter range of separation, specifically 3, 4

and 6 λ. Moreover, in order to maximize the effect of training, we reduced the visual field in which the stimulus would appear (8° in Experiment 1), placing the stimuli in one of two spatial positions, alternating between sessions. The training was conducted monocularly, so that we were able to locate the stimuli in the PRL, that maculopathy patients do not necessarily develop in the same retinal regions in the two eyes.

Method

Apparatus

Stimuli were displayed on a 19-inch Asus ML228 LCD monitor with a refresh rate of 75 Hz. The flankers and target stimuli were generated with the Matlab Psychtoolbox (Pelli, 1997; Brainard, 1997), whereas stimuli for VA and CW were generated using E-Prime software. The screen resolution was 1280 x 1024 pixels. Each pixel subtended ~1.9 arcmin. We measured CSF by using sinusoidal gratings generated by a VSG2/3 graphics card. Gratings were displayed on a 17-inch Philips Brilliance 107P CRT monitor with a refresh rate of 70 Hz and a spatial resolution of 1280 × 800 pixels. We used a gamma-corrected lookup table (LUT) so that luminance was a linear function of the digital representation of the image.

Subjects

Three maculopathy patients (MV, AG, DC) and three normal-sighted subjects (MM, CV, MG) participated in the experiments.

Subject MV (32 years old at the time of training) was diagnosed with Stargardt Syndrome and presented a central scotoma of ~ 8 deg.

Subject AG (38 years old at the time of training) was diagnosed with Stargardt Syndrome, with a central scotoma of ~ 8 deg.

Subject DC (64 years old at the time of training) was diagnosed with Age-related Macular degeneration, with a central scotoma of ~ 8 deg.

Control subjects had normal or corrected to normal vision (mean age = 24.6, SD=1.15)

Subjects sat in a dark room 57 cm from the screen. Viewing was monocular, the trained eye was the non-dominant one (the left eye for all the maculopathy subjects, the right eye for control subjects MM and MG, the left eye for control subject CV). Control subjects were instructed to fixate on a central fixation spot. Maculopathy patients were instructed to fixate the position of the screen corresponding to their PRL while maintaining the centre of their fovea aligned with the centre of the screen. All subjects gave their informed consent prior to their inclusion in the study. We have performed the study in accordance with the ethical standards laid down by the Declaration of Helsinki (1964). The study was approved by the Ethics Committee of the Department of General Psychology, University of Padua. We obtained written, informed consent from all participants involved in the study.

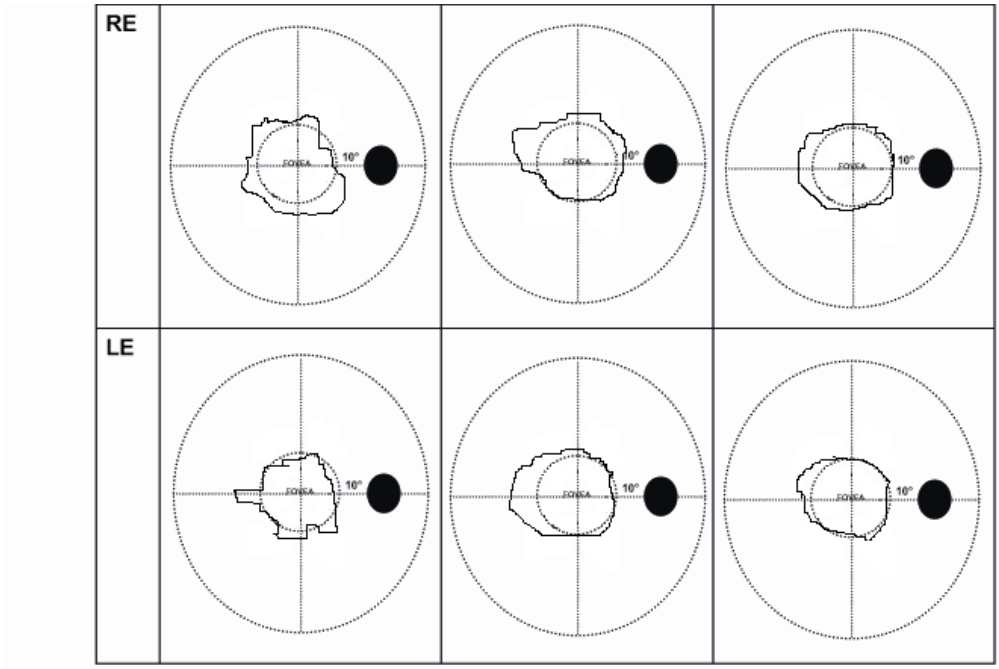
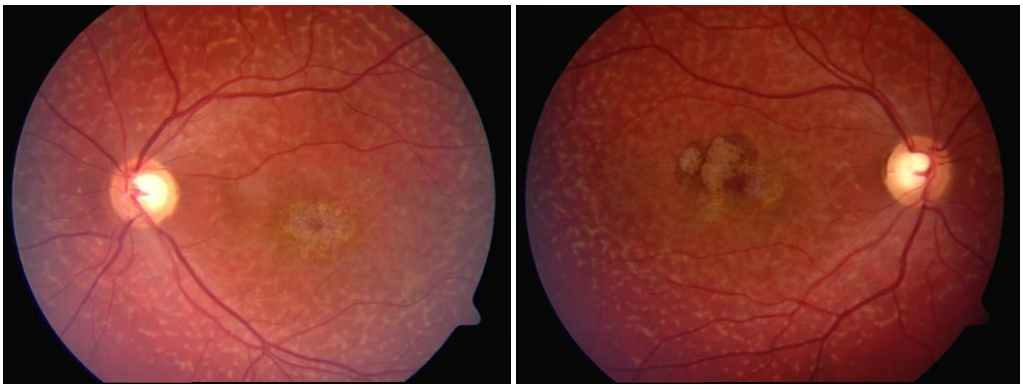
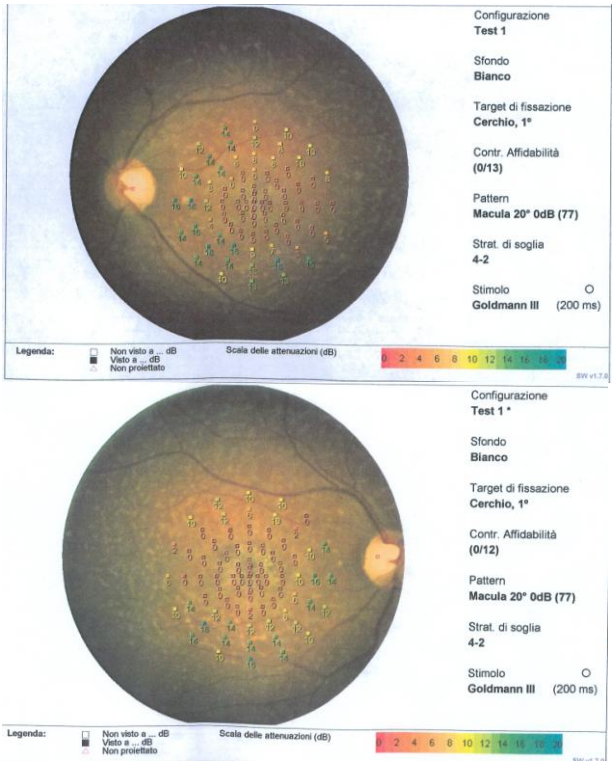


Figure 14: Area of the scotoma for both eyes of the maculopathy patients (respectively, MV, AG and DC) obtained by using microperimetry and scotometry. Describing the depressed area and locating the Preferential Retinal Locus are the first two steps in order to develop an individually tailored training.

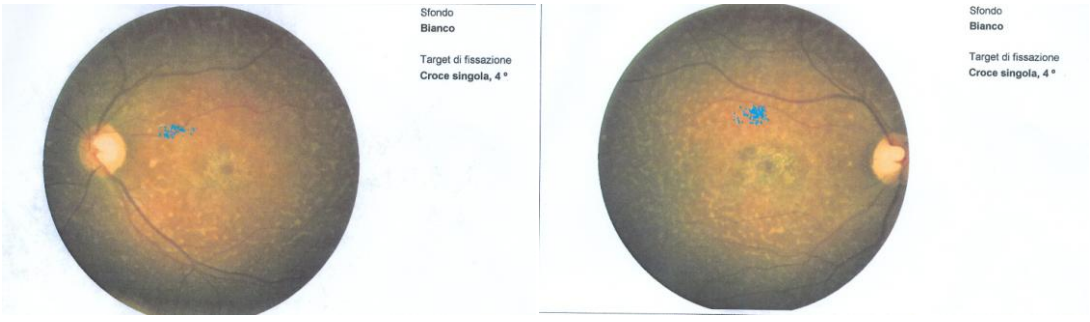
a)



b)


Configurazione
Test 1
Sfondo
Bianco
Target di fissazione
Cerchio, 1°
Contr. Affidabilità
(0/13)
Pattern
Macula 20° 0dB (77)
Strat. di soglia
4-2
Stimolo
Goldmann III (200 ms)
Legenda:
Non visto a ... dB
Visto a ... dB
Non proiettato
Scala delle attenuazioni (dB)
0 2 4 6 8 10 12 14 16 18 20
Configurazione
Test 1 °
Sfondo
Bianco
Target di fissazione
Cerchio, 1°
Contr. Affidabilità
(0/12)
Pattern
Macula 20° 0dB (77)
Strat. di soglia
4-2
Stimolo
Goldmann III (200 ms)
Legenda:
Non visto a ... dB
Visto a ... dB
Non proiettato
Scala delle attenuazioni (dB)
0 2 4 6 8 10 12 14 16 18 20

c)


Sfondo
Bianco
Target di fissazione
Croce singola, 4 °
Sfondo
Bianco
Target di fissazione
Croce singola, 4 °

d)

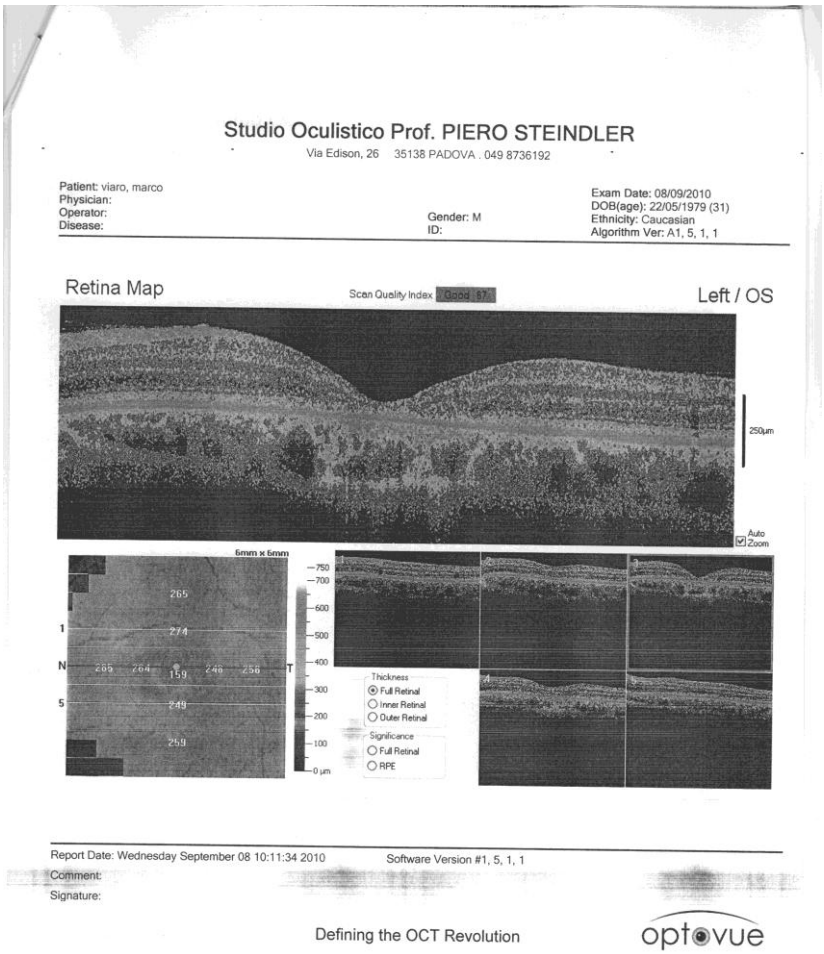


Figure 15: Examples of examinations conducted on the patients: a) angiographic exam , showing the atrophy of acular pigment epithelium and photoreceptors; b) Goldmann microperimetry, showing the area of residual view (higher numbers, green), reduced view (middle numbers, yellow) and absence of view (red); c) exam of fixation for left and right eye: the blue points indicate the part of the retina that is used by the subject during fixation tasks; d) OCT (optical coherence tomography), a high resolution technique for scanning the surface of the retina.

The examples showed here belong to subject AG, except for d), belonging to subject MV.

Location of the stimuli

Maculopathy subjects

As stated earlier, maculopathy patients spontaneously develop a new fixation point out of a peripheral retinal location, used as a functional substitute of the fovea. In order to improve the effect of learning, and studying whether the PRL presents functional differences respect to a symmetrical retinal position, we measured the location of the scotoma by using microperimetry and fixation exam in the three maculopathy subjects (Figure 11).

For subject DC, the PRL was found at 4.5 deg on the left and 3.24 deg down, for subject AG was at 5.0 deg on the left and for 4.2 deg down, for subject MV was at 3.61 deg on the left and 4.33 down.

All the maculopathy subjects presented the PRL in the lower left quadrant of the visual field.

Control subjects

For the normal-sighted subjects, in order to establish a reliable comparison group, we located stimuli in a position that was approximately at a similar distance from the fovea as for the maculopathy subjects. Therefore, the "PRL configuration" (that clearly, for non-maculopathy patients, indicates only a non-specific peripheral location) was set at 4 deg on the left and 4 deg down, while the "No-PRL configuration" was set at 4 deg on the left and 4 deg up.

Training stimuli

Stimuli were Gabor patches consisting of a cosinusoidal carrier enveloped by a stationary Gaussian. The mean luminance of the display was 46.7 cd/m_2. Each Gabor patch was characterized by its sinusoidal wavelength λ, phase φ, and SD of the luminance Gaussian envelope (σ) in the (x, y) space of the image:

$$G(x, y) = \cos(2\pi / \lambda x + \varphi) \exp(-(x^2 + y^2) / \sigma^2) \qquad \text{Eq.1}$$

In all experiments, σ = λ and φ = 0 (even symmetric). Gabors had a spatial frequency of 2 and 3 cpd. For maculopathy patients, the location of the target relative to the fixation point (0.18 deg) was in the point of the visual field corresponding to the Preferential Retinal Locus of each subjects, measured individually (roughly 4 deg up and 4 deg right respect to the fixation point) and in a symmetrical locus (defined as "No-PRL"), varying between blocks. For normal-sighted subjects, the location of the configurations was at 4 deg up and 4 deg right or 4 deg down and 4 deg right respect to the fixation point, in separate blocks. In each training session the position of the configuration was always the same (i.e. PRL or No-PRL). A vertical Gabor target (Figs. 12A and 12B, respectively) was presented flanked, above and below, by two high-contrast Gabor patches (0.6 Michelson contrast). During the learning session, the flankers were always vertically oriented and located at various distances from the target (i.e., 3λ, 4λ, and 6λ). For each subject, and for each spatial frequency and spatial position condition, we used a 1up/3down Leavitt staircase in order to obtain a contrast value corresponding to 80% of correct detection, then we selected 2 contrast values 0.2 log step above and 2 contrast values 0.2 log step below this 80% thresholds for defining the contrast values in the Constant Stimuli procedure used for the training sessions. Moreover, we used an additional contrast level of 0.0 (Michelson contrast) in order to introduce "catch trials" to estimate the false alarms rate.

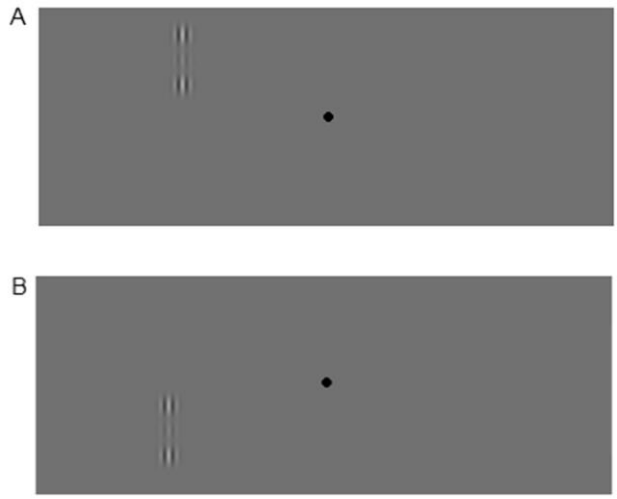


Figure 16: configuration used for Experiment 3: differently from Experiment 1 and Experiment 2, in Experiment 3 we modified eccentricities also for the y axis, in order to locate the triplet of the stimuli within the PRL of each subject. A: PRL condition; B: No-PRL condition

VA and CW stimuli

The stimuli were 10 randomly chosen alphabet letters (D, N, S, C, K, R, Z, H, O, V) that were each presented for a duration of 133 ms. In the VA test, the location of the target letter was in the PRL of each maculopathy subject or in the symmetric retinal location (No-PRL), in separate blocks, leading to two different measurements for Visual Acuity. The size of the letters varied according to a 1up/3down staircase (Levitt, 1971). The step size was 0.186 arcmin (vertical font streak), , the character type was Arial, and the starting size for the letter was 3.72 arcmin Subjects had to say the letter displayed and the experimenter registered the answer. The session terminated after either 100 trials or 8 reversals. A threshold acuity, expressed as the font size for 79% correct identifications, was the mean of the 8 reversals.

In the CW test, the target letter was flanked on the left and the right sides by two different letters. The triplets could appear randomly either to the left or to the right of the fixation point, but the target letter was always at 4 deg from the fixation spot. In the CW test, the size of both the target letter and flanking letters was set 20% larger? than the VA threshold. Inter-letter distance varied according to a 1up/3down staircase (Leavitt, 1971). The initial distance between letters was set at 95 arcmin, and the step

size was constant at 1.9 arcmin. The session terminated either after 100 trials or 8 reversals. At the end of the procedure, we calculated the threshold by averaging the distance values in correspondence with the 8 reversals.

CSF stimuli

We measured peripheral CSF with vertical gratings displayed on the whole screen area except for the fovea. This was carried out by placing a circular black spot (4° radius, the same eccentricity used for stimuli presentation in the training sessions) at the centre of the screen to force subjects to attend the near-periphery of their visual field while fixating on the center of the dark spot. Individual contrast thresholds were estimated with the Method of Limits over seven spatial frequencies (0.1, 0.2, 0.4, 0.9, 2.0, 4.5, and 10.2 cpd).

Procedure

Contrast sensitivity functions (CSF), visual acuity test (VA) and crowding test (CW), in addition to contrast thresholds for the lateral interaction task, with both collinear and orthogonal flankers, were measured initially to establish individual baseline performances and after the training period. We tested lateral interactions by comparing the contrast detection of a vertical Gabor target (2 and 3 cpd) flanked by either two vertically oriented Gabor patches (collinear condition – Fig. 12A) or two horizontal Gabors (orthogonal condition – Fig. 12B) with target-to-flankers distances of 3λ, 4λ, and 6λ. The contrast detection threshold was measured for the target Gabor presented at 4 deg of eccentricity. Each stimulus was presented for 133 ms.

A standard training block consisted of a contrast-detection task on the central Gabor patch flanked by two high-contrast and collinear Gabor patches. A typical daily session consisted of twelve blocks, in which the target-to-flankers distance varied, starting from the highest distance (6λ) and the lowest spatial frequency (2 cpd), with presentation in the PRL and in the No-PRL in separate blocks. A weekly session consisted of three consecutive daily sessions. Each daily session consisted in 384 trials separated in 12 blocks: experimental block consisted of 48 trials that corresponded to 8 repetitions of 12 stimuli condition (2 spatial frequencies x 2 retinal position x 3 target-to-flankers

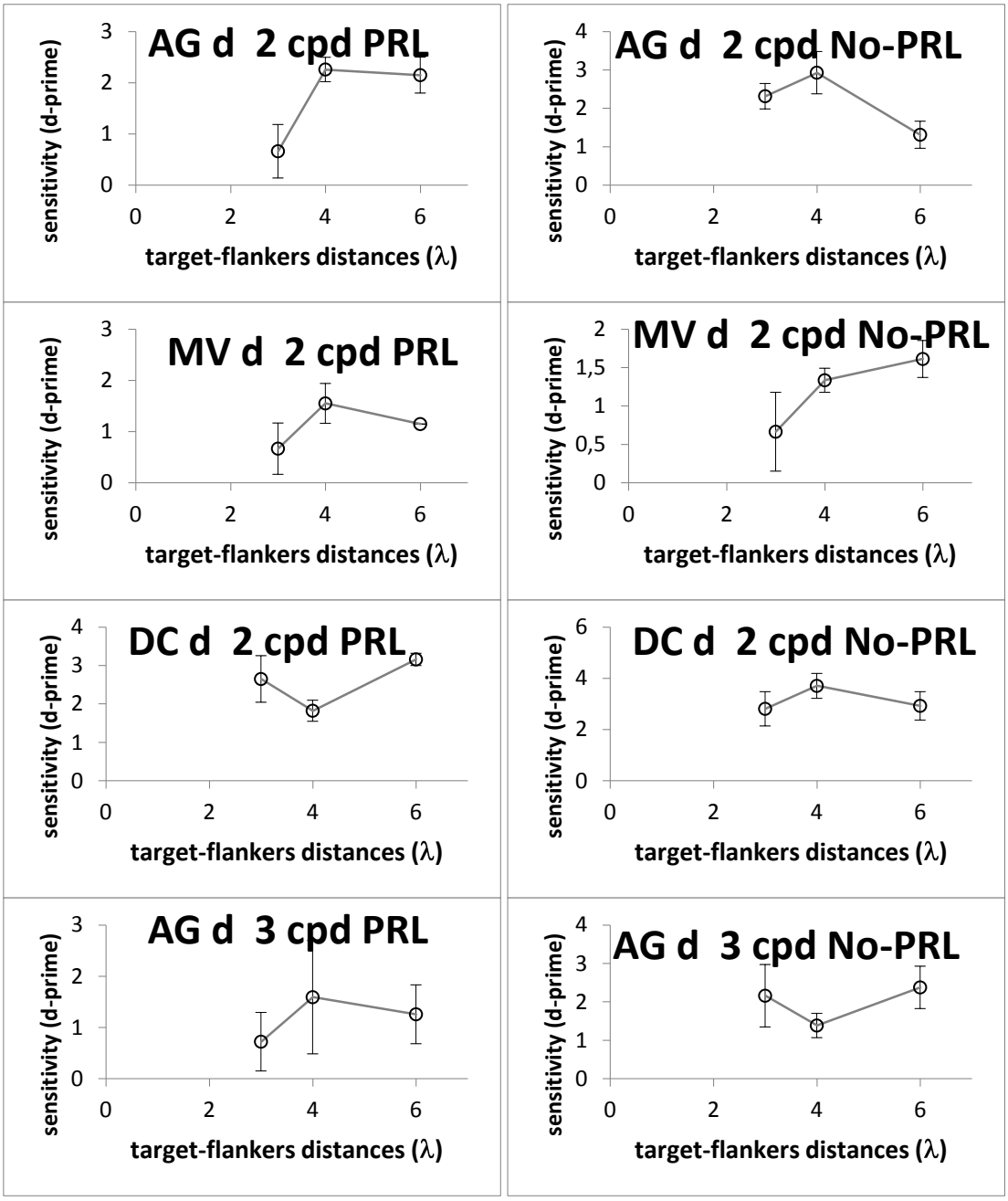
distances). The Method of Constant Stimuli and a yes/no detection paradigm were used. Globally, each subject performed 288 sessions distributed over the course of 8 weeks. For all the comparisons, we used Student's t-tests.

Results

Lateral masking curves

Differently from Experiment 1 and Experiment 2, in Experiment 3 pre and post tests contrast thresholds measured with the yes/no paradigm and the 3 up/ 1 down staircase (Levitt, 1971) did not result in solid measurements. The high number of false alarms during the pre and post tests sessions produced extremely low, unreliable thresholds. As a consequence, instead of using contrast threshold measured in pre and post tests, we measured detection sensitivity for the first and the last week of training, as we did for Experiment 1, according to the Signal Detection Theory. We considered as Hits the correct detection of the flanked target presented at the second highest contrast value used in the Constant Stimuli procedure during the training, as in Experiment 1. The main negative effects of this lack of reliability is that we cannot compare measurements for collinear and orthogonal conditions, since the training was carried only on the former, and consequently no d-prime can be calculated for the latter.

Maculopathy Subjects


AG d 2 cpd PRL
AG d 2 cpd No-PRL
MV d 2 cpd PRL
MV d 2 cpd No-PRL
DC d 2 cpd PRL
DC d 2 cpd No-PRL
AG d 3 cpd PRL
AG d 3 cpd No-PRL
sensitivity (d-prime)
target-flankers distances (λ)

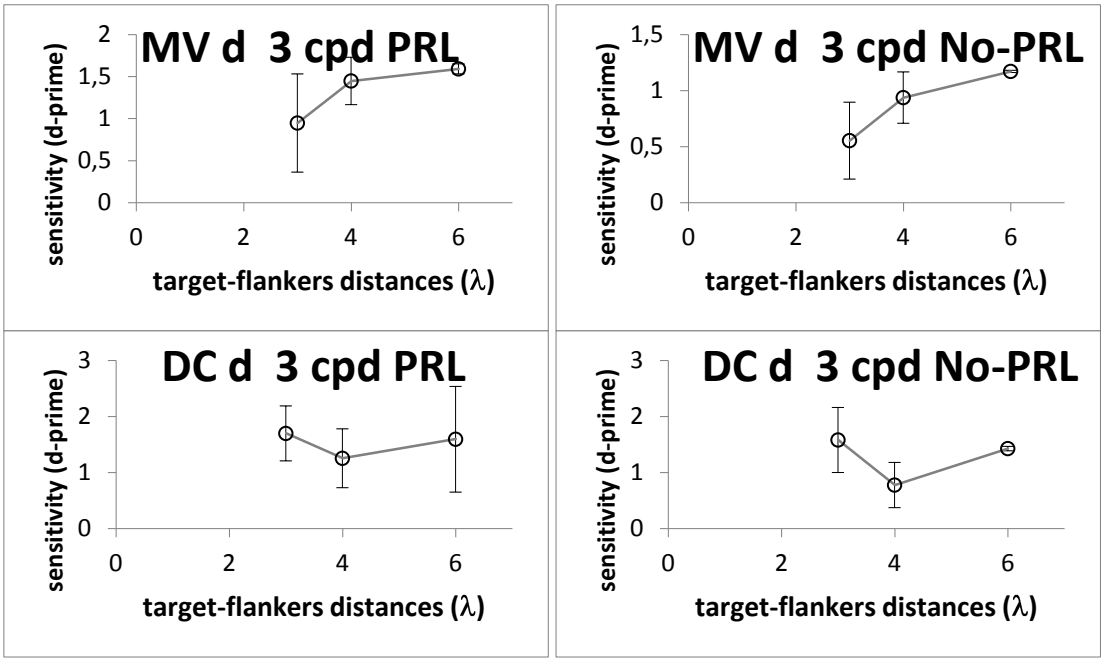


Figure 17: Sensitivity for the contrast detection task in the pretest (Maculopathy subjects)

Mean d-prime of the first week of training plotted as a function of the target-to-flanker distances (λ).

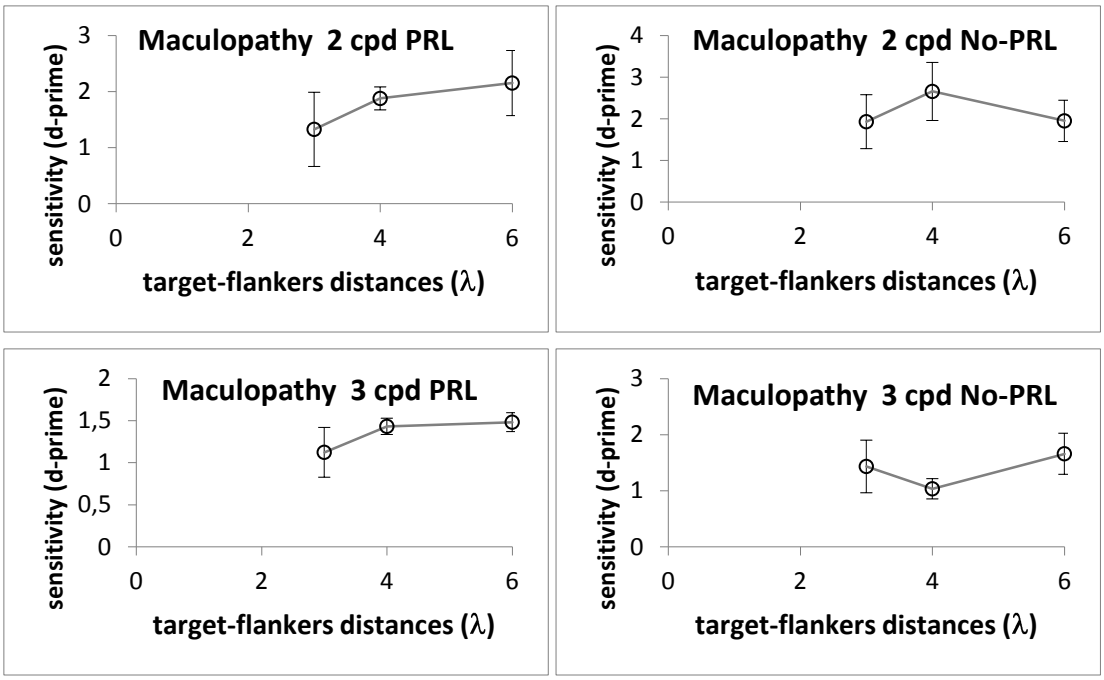
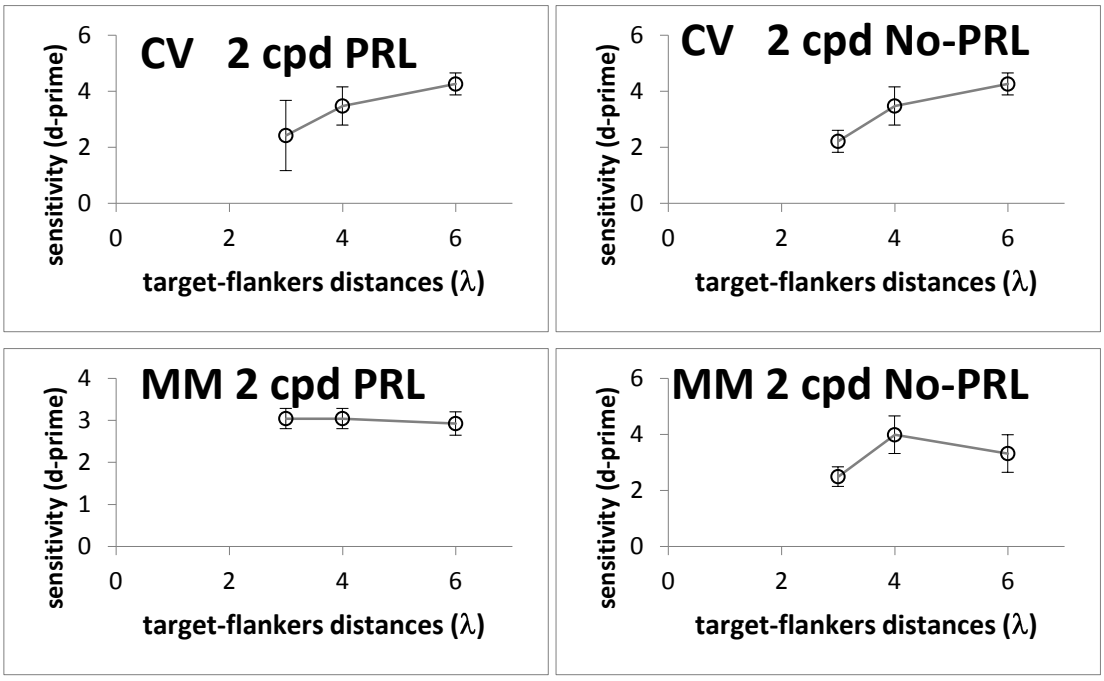


Figure 18: mean of Sensitivity for the contrast detection task in the pretest (Maculopathy subjects)

Mean d-prime of the first week of training plotted as a function of the target-to-flanker distances (λ).

In general, for maculopathy patients, except for the condition with the highest spatial frequency and location of the stimuli at the No-PRL, detection sensitivity seems to increase with the distance of the flankers. Interestingly, detection in the PRL does not seem better than in a symmetrical retinal locus of the retina, a result that is consistent with the hypothesis of Dilks et al. (2009) concerning the absence of specificity for the PRL in the cortical reorganization of maculopathy patients.

Control Subjects



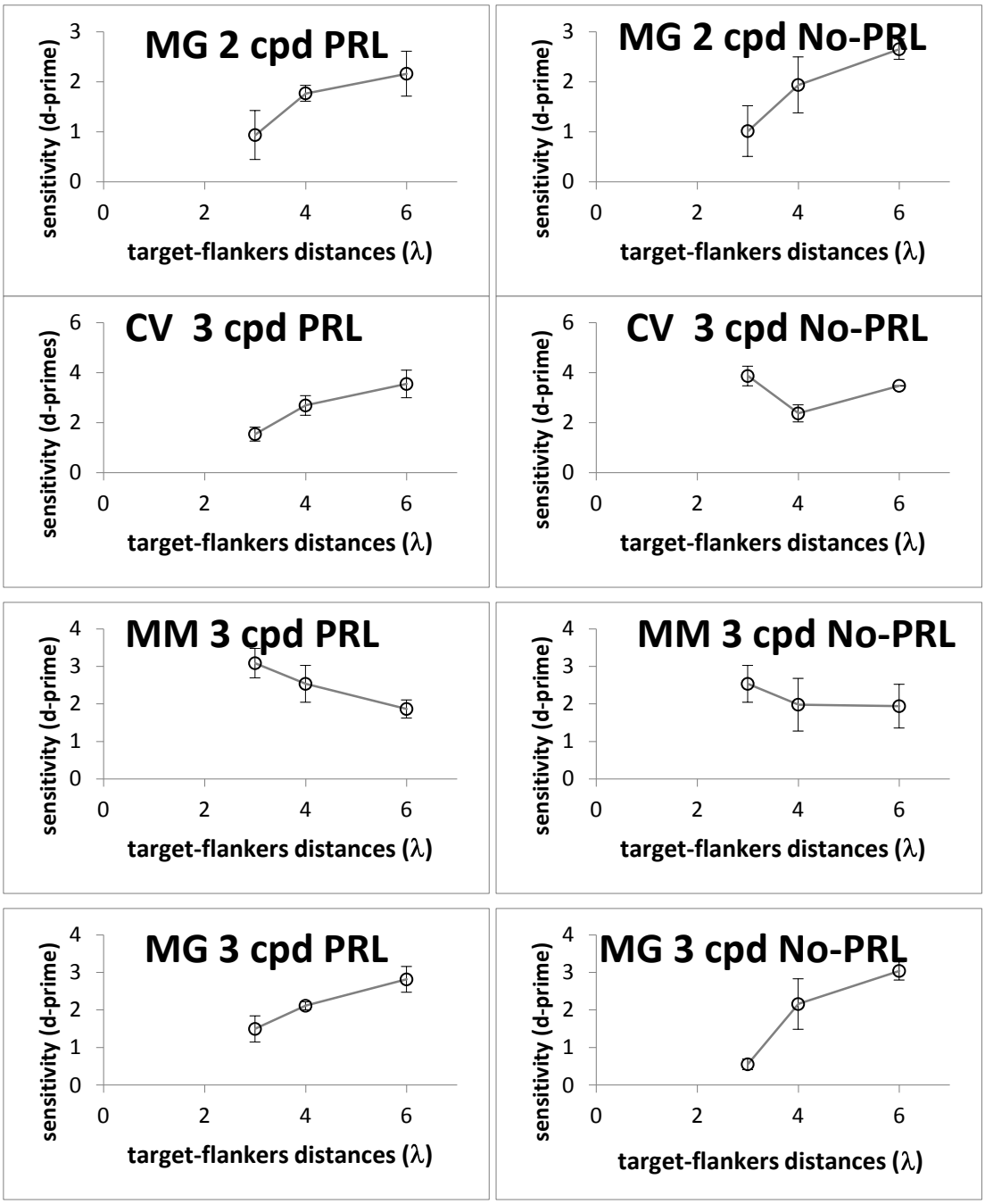


Figure 19: Sensitivity for the contrast detection task in the pre tests (Control subjects)

Mean d-prime of the first week of training plotted as a function of the target-to-flanker distances (λ).

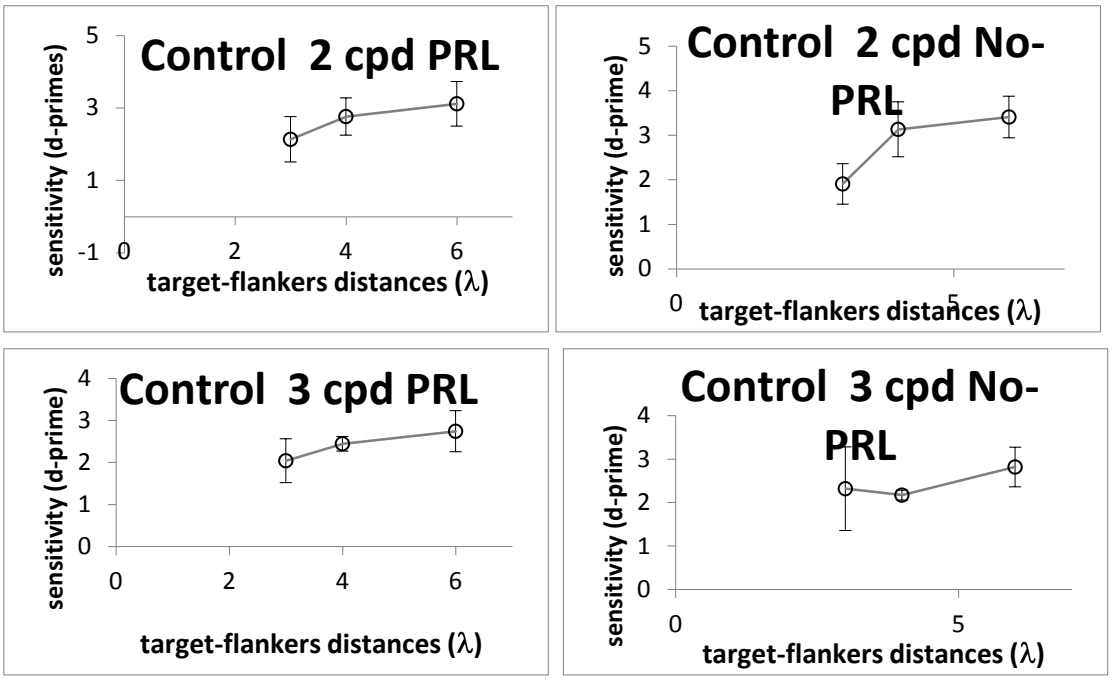


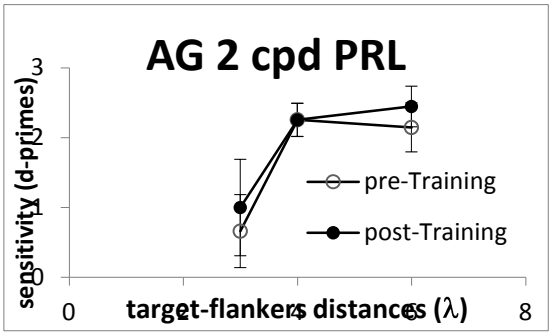
Figure 20: mean of Sensitivity for the contrast detection task in the pre test (Control subjects)
Mean d-prime of the first week of training plotted as a function of the target-to-flanker distances (λ).

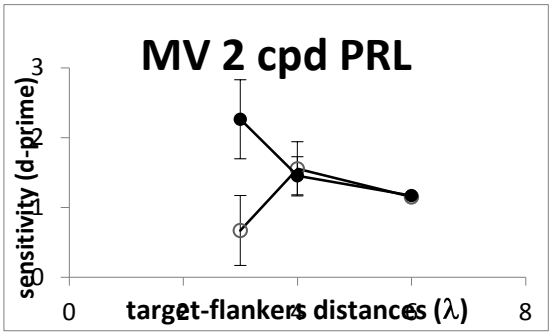
Similarly to the maculopathy group, control subjects show in general, a higher sensitivity with increasing target-to-flankers separations.

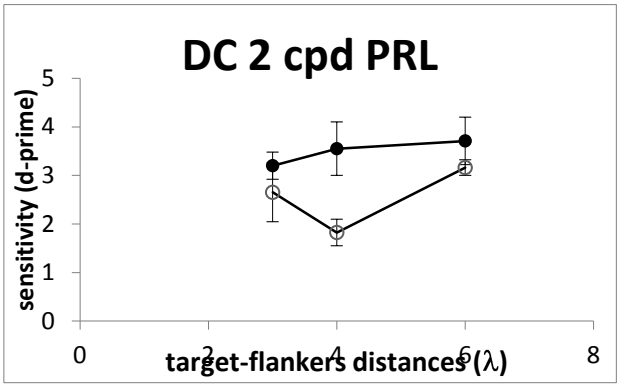
Perceptual learning

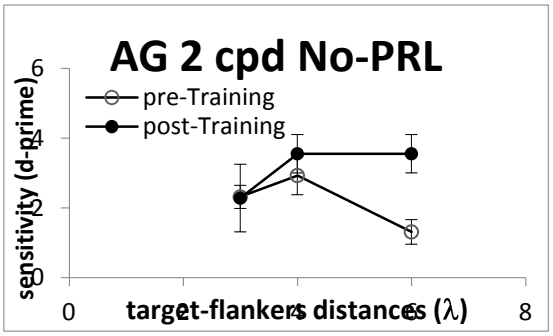
In general, the trend of perceptual learning is towards the direction of a improvement of detection sensitivity for the detection of a collinearly flanked target for both groups, even though few conditions reached significancy.

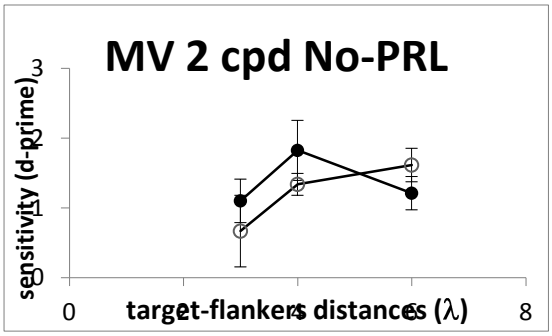
Maculopathy Subjects

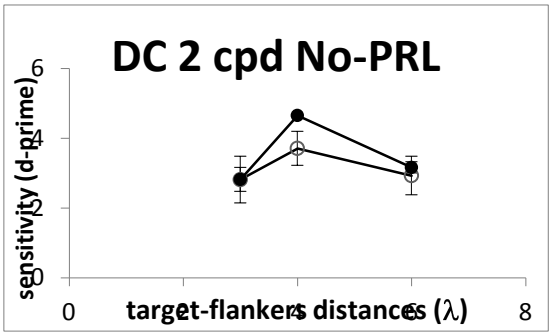

AG 2 cpd PRL
sensitivity (d-primes)
target-flankers distances (λ)
pre-Training
post-Training


MV 2 cpd PRL
sensitivity (d-prime)
target-flankers distances (λ)


DC 2 cpd PRL
sensitivity (d-prime)
target-flankers distances (λ)


AG 2 cpd No-PRL
sensitivity (d-prime)
target-flankers distances (λ)
pre-Training
post-Training


MV 2 cpd No-PRL
sensitivity (d-prime)
target-flankers distances (λ)


DC 2 cpd No-PRL
sensitivity (d-prime)
target-flankers distances (λ)

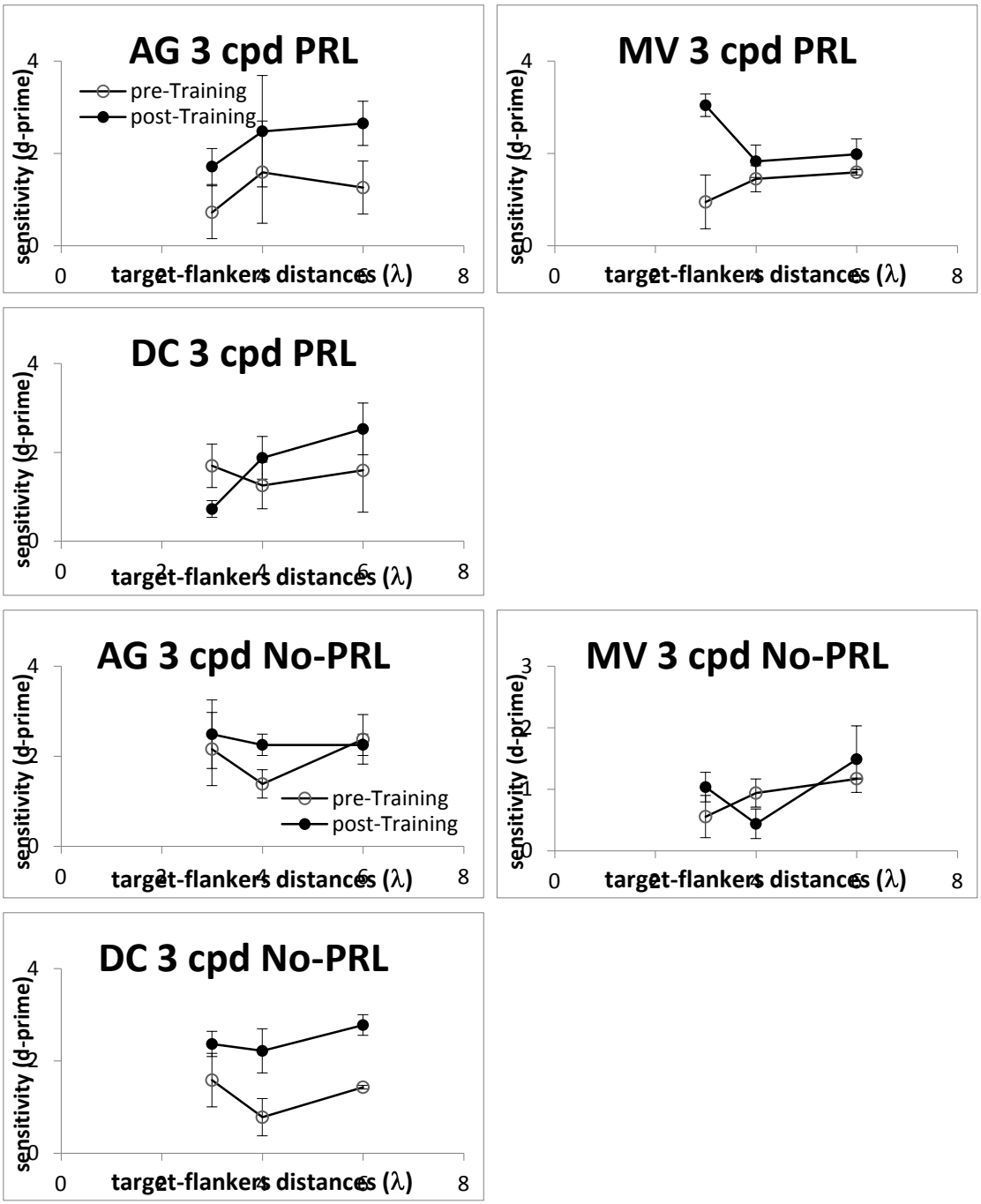


Figure 21: Sensitivity for the contrast detection task before and after training (Maculopathy subjects). Mean d-prime of the first week of training (filled circles) and from the last week (open circles) plotted as a function of the target-to-flanker distances (λ).

In subject MV, training improved sensitivity for the target with spatial frequency of 3 cpd and target-to-flankers distance of 4λ ($t3 = 4.539$, $p = .045$).

In subject AG, training was effective in improving contrast detection for the flanked target with spatial frequency of 3 cpd ad separation of 6 λ (t3 = 13.182, p = .006).
In subject DC, training improved sensitivity for the target with spatial frequency of 3 cpd and target-to-flankers distance of 6λ (t3 = 5.479, p = .032).

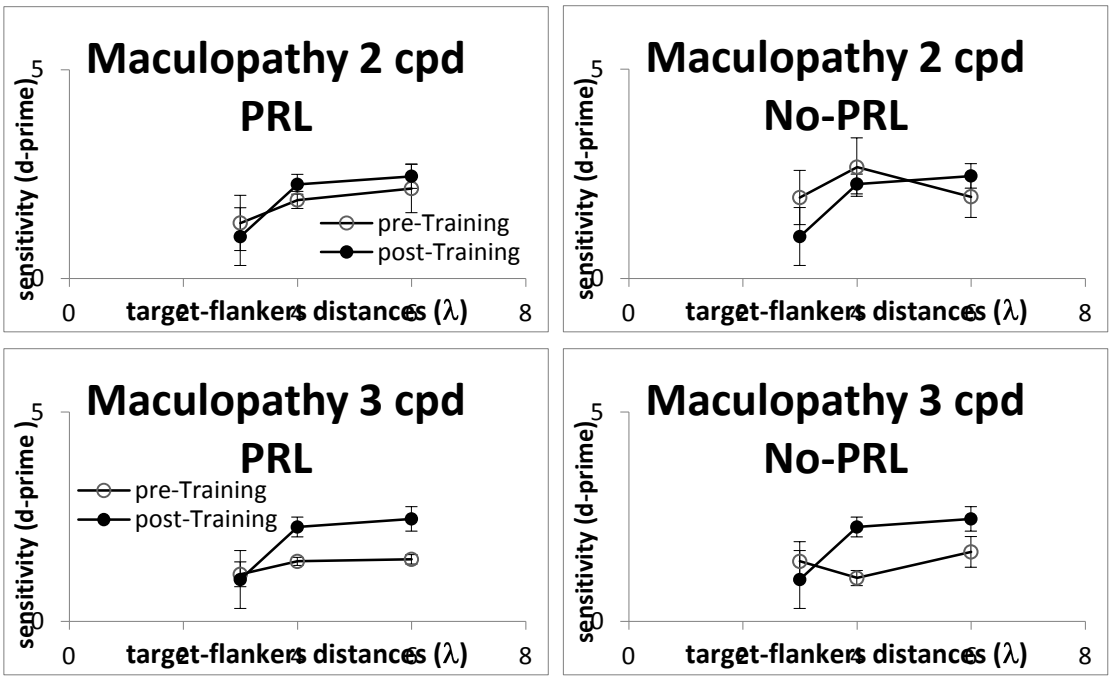
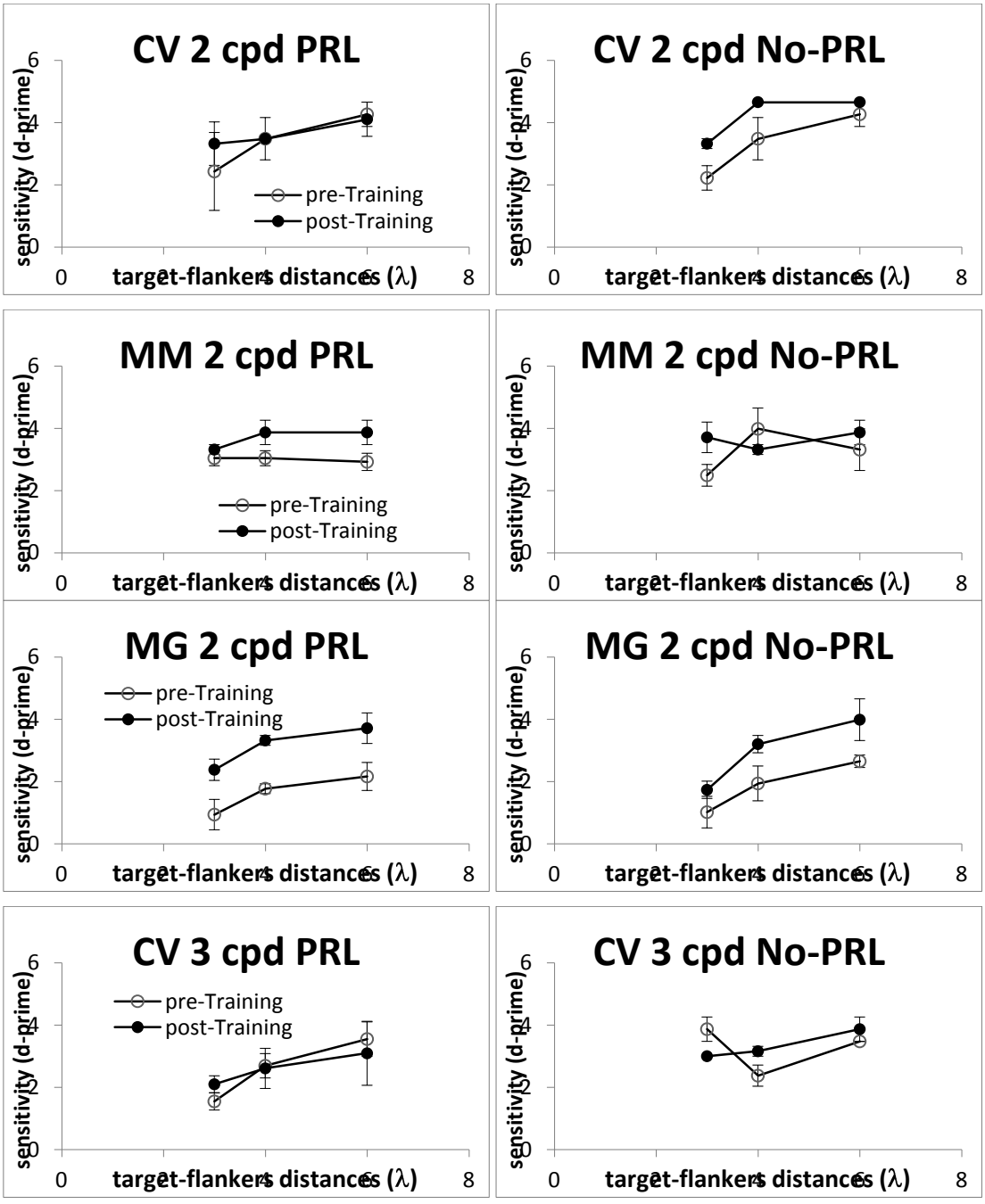


Figure 22: Mean Sensitivity for the contrast detection task before and after training (Maculopathy subjects). Mean d-prime of the first week of training (filled circles) and from the last week (open circles) plotted as a function of the target-to-flanker distances (λ).

Considering the average performance of the maculopathy group in pre and post tests, we found a significant improvement in detection sensitivity for target with 2 cpd and 4 λ in the No-PRL (t3 = 5.061, p = .037) and for the condition in which target had 3 cpd of spatial frequency and target-to-flankers separation of 4 λ in the PRL (t3 = 4.319, p = .049).

Control Subjects



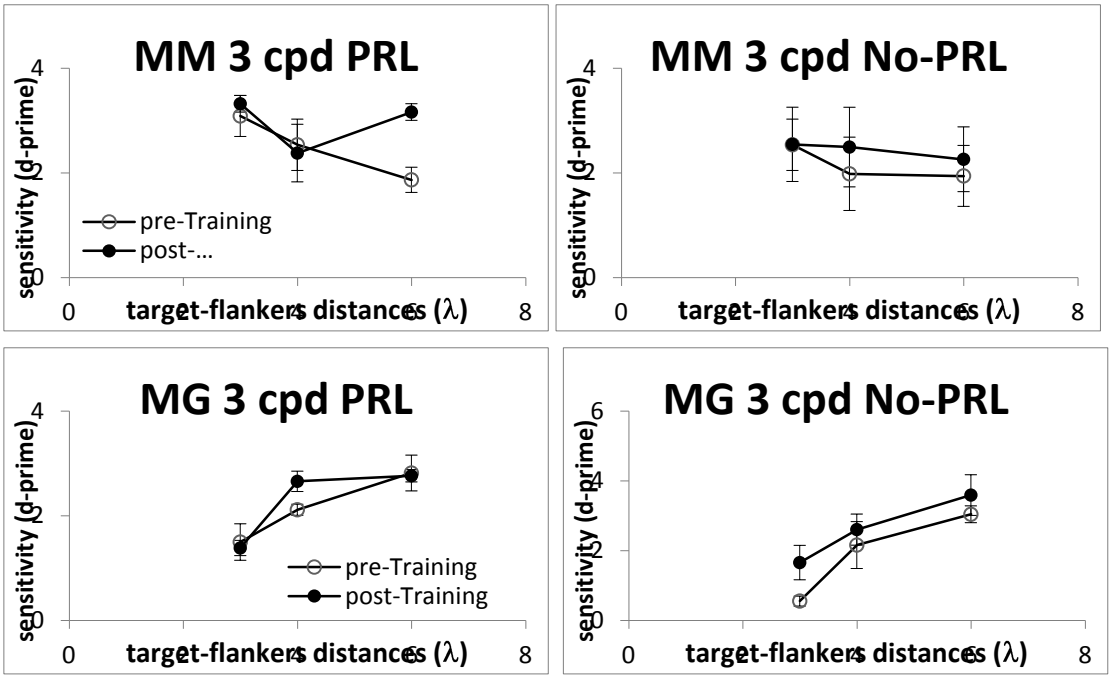
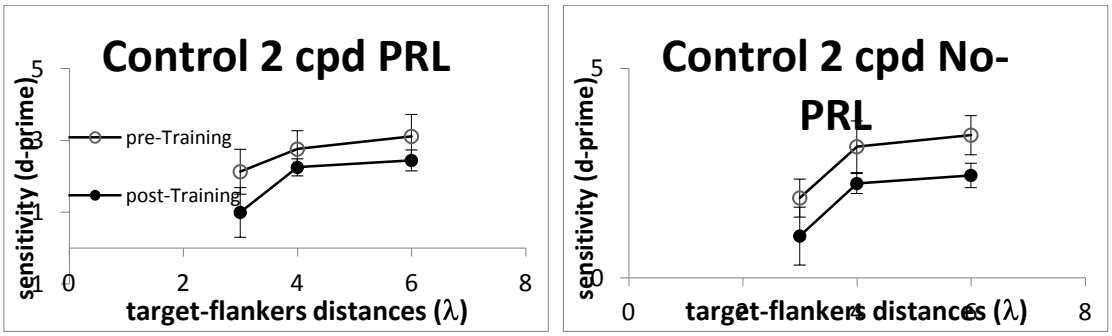


Figure 23: Sensitivity for the contrast detection task before and after training (Control subjects)
Mean d-prime of the first week of training (filled circles) and from the last week (open circles) plotted as a function of the target-to-flanker distances (λ).

In subject MM, training resulted effective in improving sensitivity with a 3 cpd target with flanker located at 6 l, in the PRL location (t3 = 8.247, p = .014)

In Subject MG, training produced an increase of sensitivity at 2 cpd 4 λ in the PRL position

(t3 = 6.368, p = .024)



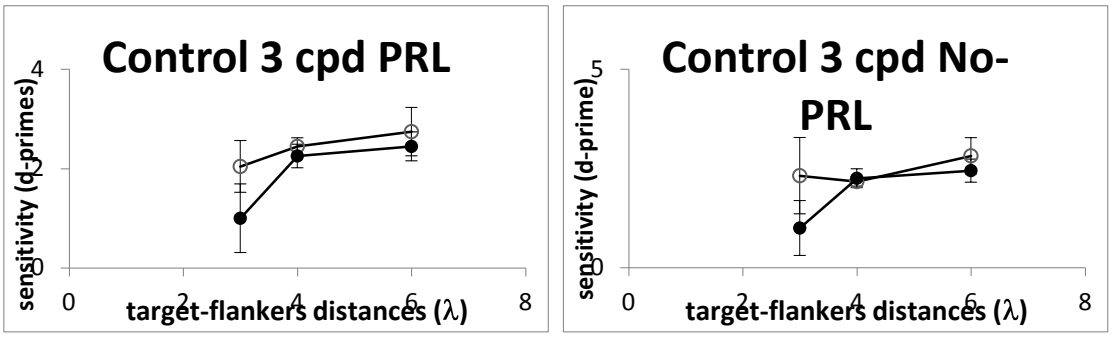


Figure 24: Mean Sensitivity for the contrast detection task before and after training (Control subjects). Mean d-prime of the first week of training (filled circles) and from the last week (open circles) plotted as a function of the target-to-flanker distances (λ).

Considering the average performance of the control group in the and post tests, we found a significant improvement in detection sensitivity for target with 2 cpd and 4 λ in the No-PRL ($t3 = 6.702$, $p = .022$) and for the condition in which target had 3 cpd of spatial frequency and target-to-flankers separation of 4 λ in the No-PRL ($t3 = 5.802$, $p = .028$). The absence of a more clear evidence for sensitivity improvement after training could be attributed, at least partially, to a "roof effect", since some subjects showed high d-prime already in the pre test. Moreover, the number of subjects for the two groups was small. Hoverer, the trend is toward the improvement of sensitivity after training.
As a general conclusion, training seems more effective in improving sensitivity at the larger target-to-flankers distances tested and for the higher spatial frequency used.

Transfer of learning to CSF

For measuring the transfer of learning from the contrast detection training to the contrast sensitivity function, as in Experiment 1, we compared performances in the pre e post test separately for the two group of subjects.

Maculopathy Subjects

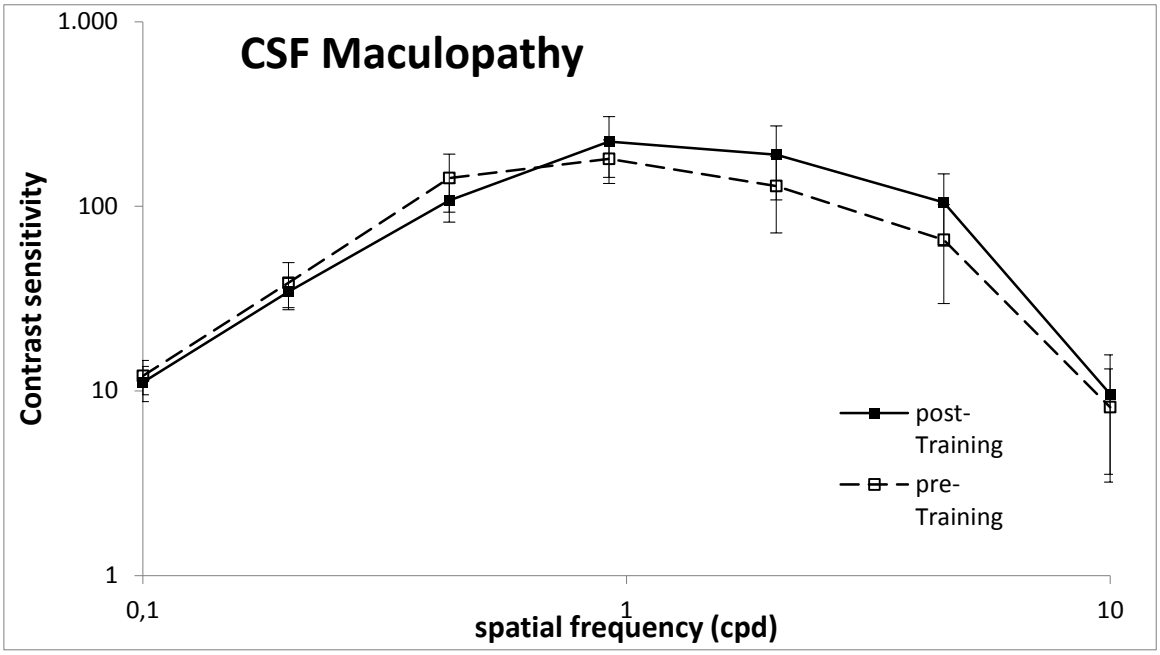


Figure 25: Contrast sensitivity functions for the Maculopathy subjects. Mean CSFs measured before and after training

For maculopathy patients, no significant improvement is reported for the contrast sensitivity function, although a tendency can be seen towards the higher (not directly trained) spatial frequencies.

Control Subjects

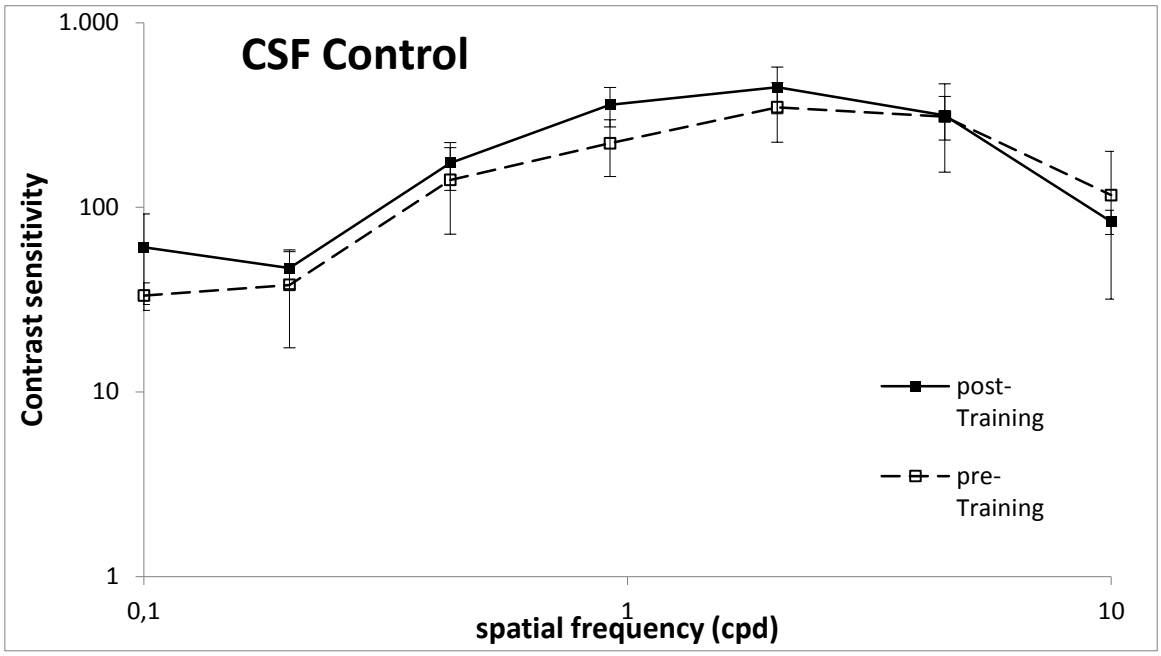


Figure 26: Contrast sensitivity functions for the Control subjects. Mean CSFs measured before and after training

For the control subjects, contrast sensitivity improved significantly at 1 cpd ($t2 = 4.908$, $p = .039$), with a general trend towards improvement for almost all the tested spatial frequencies.

In general, although not significant, the Contrast Sensitivity Functions tend to be higher for both groups for the medium-high spatial frequencyies

Transfer of learning to VA

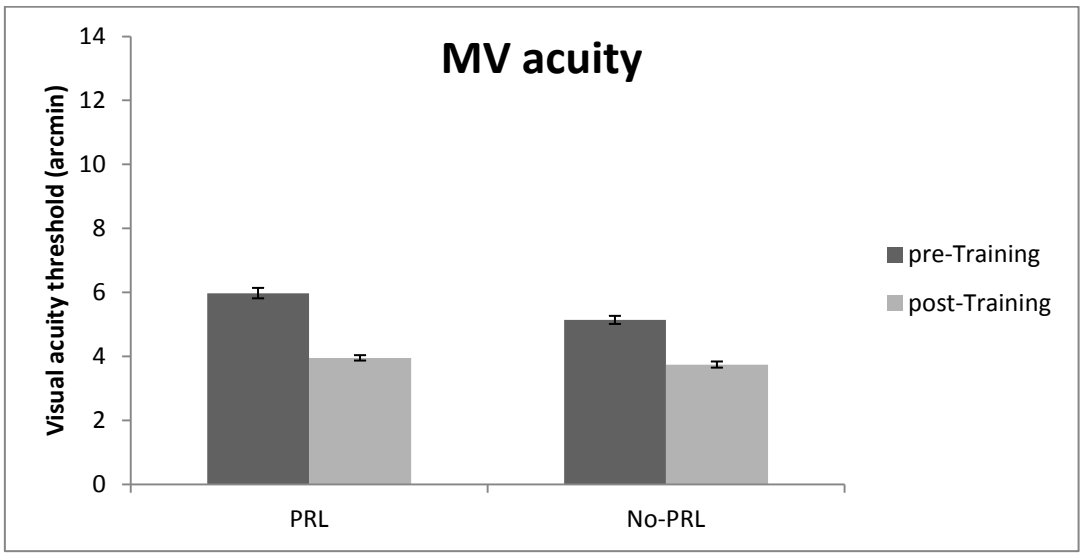
For measuring the transfer of learning to visual acuity, we compared the last 8 reversals of the pre- measurements (3up/1 down Leavitt staircase) with the last 8 reversals of the post test, individually for each subject.

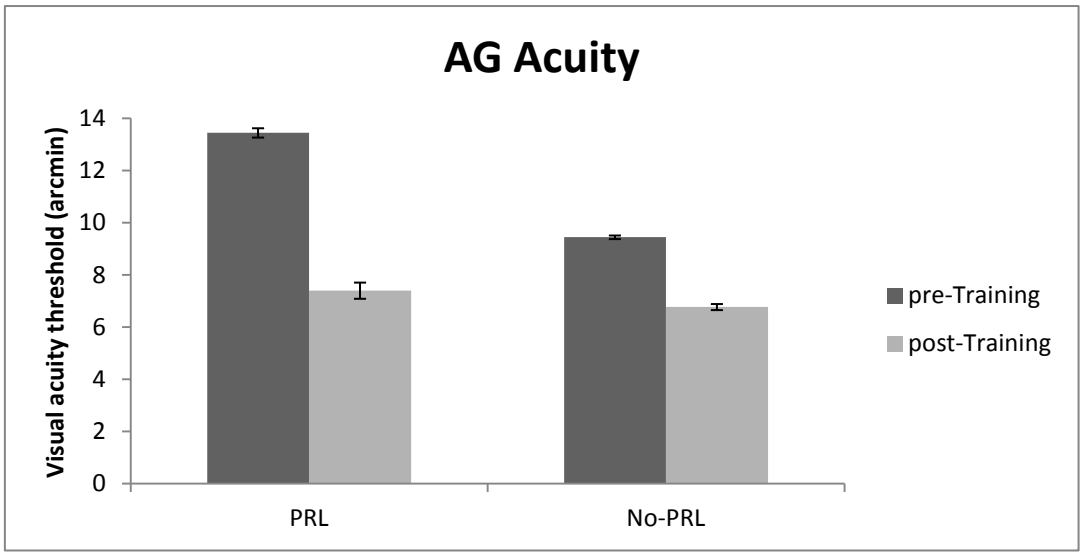
Maculopathy Subjects

For all the Maculopathy subjects, training on contrast detection transfers to visual acuity both for PRL and no-PRL training sites: MV: no-PRL: $t7 = 6.806$, $p < .0001$ PRL: $t7 = 15.698$, $p < .0001$.

AG: PRL: $t7 = 20.128$, $p < .0001$; no-PRL: $t7 = 31.217$, $p < .0001$.

DC: PRL: $t7 = 10.139$, $p < .0001$; no-PRL: $t7 = 34.000$, $p < .0001$.





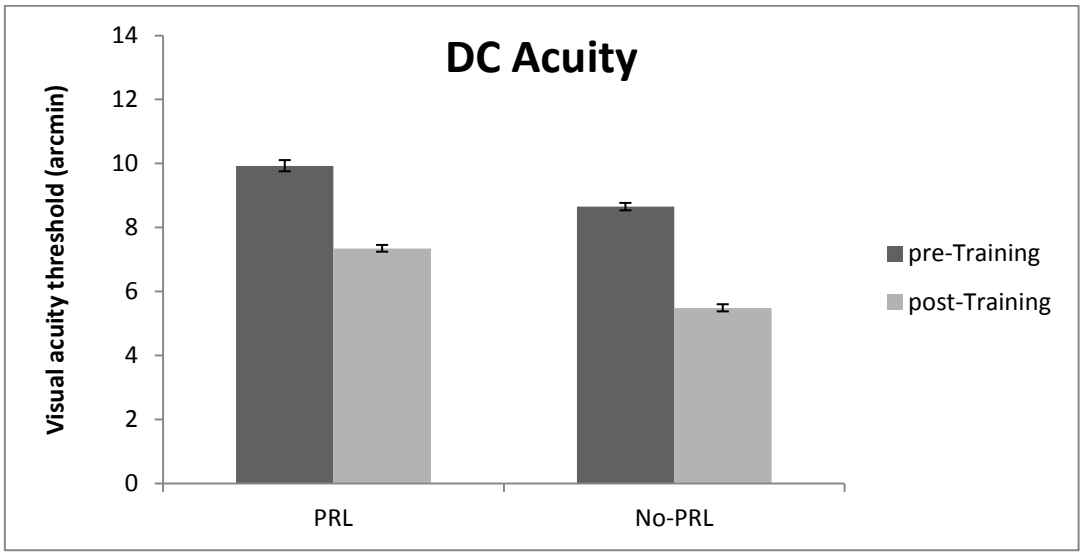
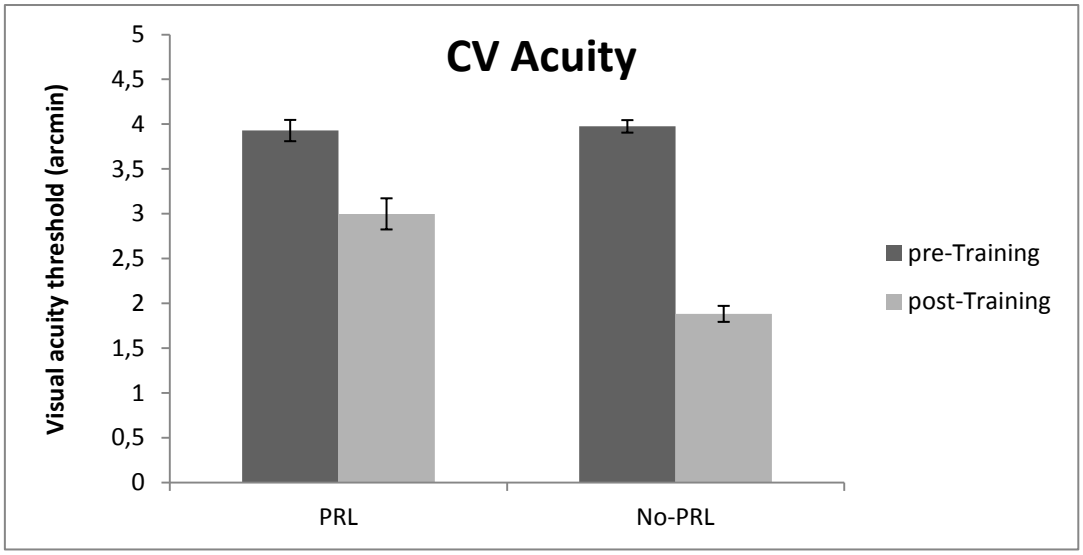


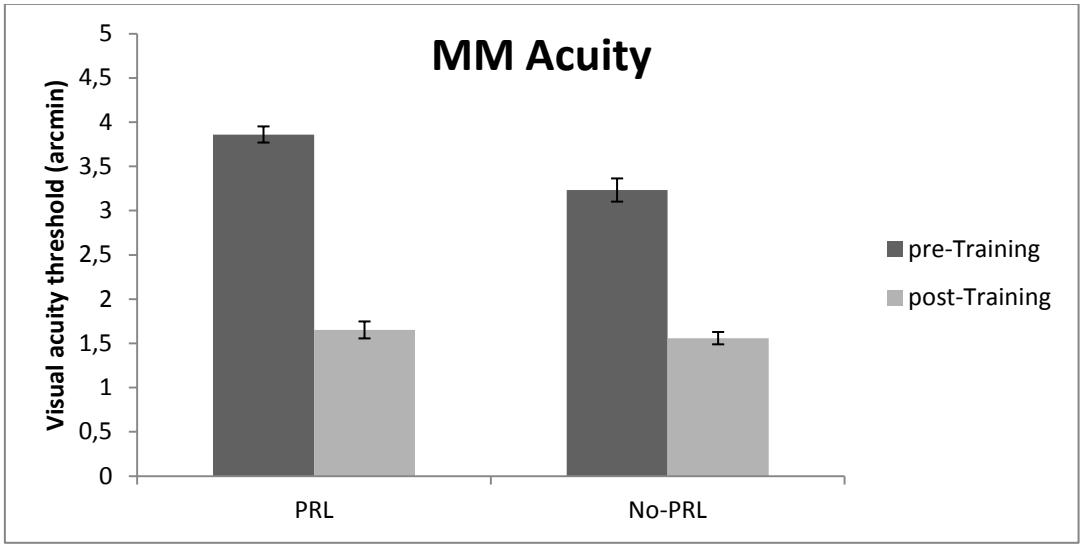
Figure 27: Visual Acuity thresholds before and after training for Maculopathy subjects. Error bars ± 1 s.e.m.

What is interesting to notice is that pre test performance on Visual Acuity, for all the maculopathy subjects, showed a better performance in the No-PRL respect to the PRL. Moreover, training seems to be effective in a similar way for the two retinal positions. These results, as the one of the perceptual learning, point in the direction of the functional similarity between PRL and other peripheral retinal loci.

Control Subjects

For subject CV, training on contrast detection transferred to visual acuity both for PRL and no-PRL training sites (PRL: $t7 = 4.035$, $p = .005$; no-PRL: $t7 = 14.545$, $p < .0001$).
For subject MM, training on contrast detection transferred to visual acuity both for PRL and no-PRL training sites (PRL: $t7 = 13.571$, $p < .0001$; no-PRL: $t7 = 21.298$, $p < .0001$).
For subject MG, training on contrast detection transferred to visual acuity for PRL (PRL: $t7 = 6.335$, $p < .0001$), while for the no-PRL, the visual acuity worsened (no-PRL: $t7 = 3.464$, $p = .01$).


CV Acuity
Visual acuity threshold (arcmin)
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5
0
PRL
No-PRL
pre-Training
post-Training


MM Acuity
Visual acuity threshold (arcmin)
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5
0
PRL
No-PRL
pre-Training
post-Training

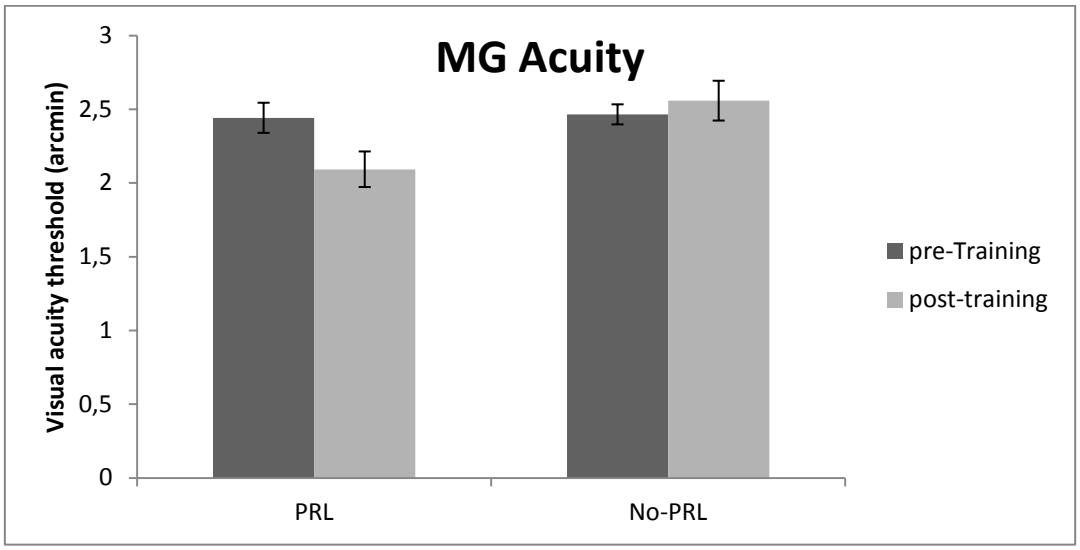


Figure 28: Visual Acuity thresholds before and after training for Control subjects. Error bars ± 1 s.e.m.

For 2 of the 3 control subjects, training improved peripheral visual acuity in both PRL and No-PRL.

Curiously, for subject MG, while training improved vision in the PRL, it worsened performance in the No-PRL. This is a new result respect to Experiment 1, in which no transfer to Visual Acuity were found. This effect could be due to the reduction of spatial areas that subjects had to attend, consequently forcing them to focus on a limited portion of space (reduction of spatial uncertainty). As Freeman et al. (2001) showed in foveal vision and Shani and Sagi (2005) partially confirmed for the periphery of the visual field, allocation of attention is crucial in the manifestation of collinear interaction modulations. Consequently, the focusing of attention could have improved the transfer of learning to Visual Acuity.

Transfer of learning to CW

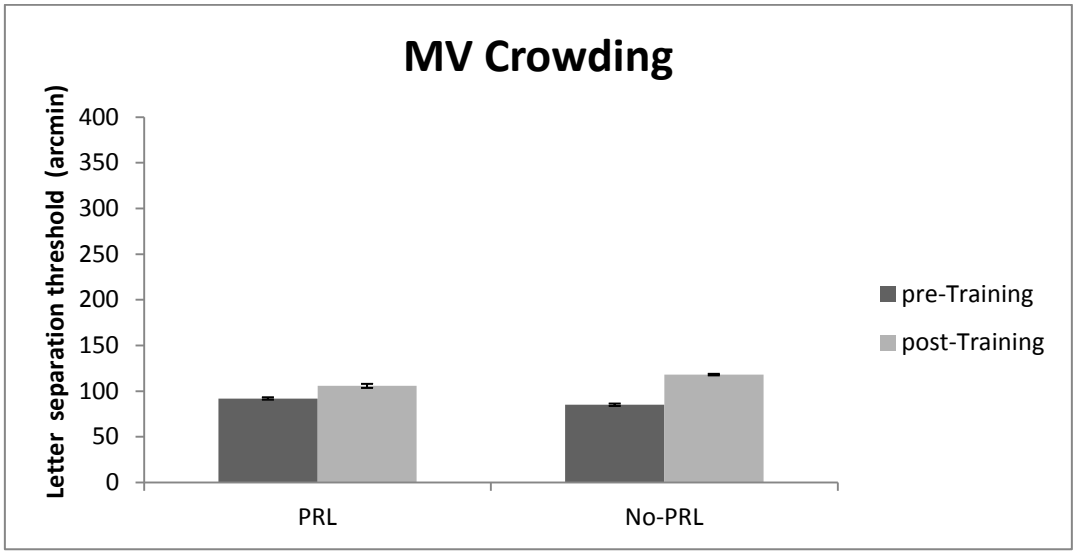
For measuring the transfer of learning to crowding reduction, we compared the last 8 reversals of the pre test measurements (the 3up/1 down Leavitt staircase) with the last 8 reversals of the post test, individually for each subject.

Maculopathy Subjects

For subject MV, training on contrast detection did not result in a crowding reduction, but in an increase of critical space for both for PRL and no-PRL training sites (no-PRL: $t7 = 23.3$, $p < .0001$; PRL: $t7 = 9.989$, $p < .0001$).

For subject AG, training on contrast detection transfers to crowding reduction for the No- PRL ($t7 = 47.446$, $p < .0001$) but not for the PRL ($t7 = 1.759$, $p = .122$).

For subject DC, training on contrast detection transfer to crowding reduction for both for PRL and no-PRL training sites (PRL: $t7 = 3.632$, $p = .008$; no-PRL: $t7 = 2.956$, $p < .021$).



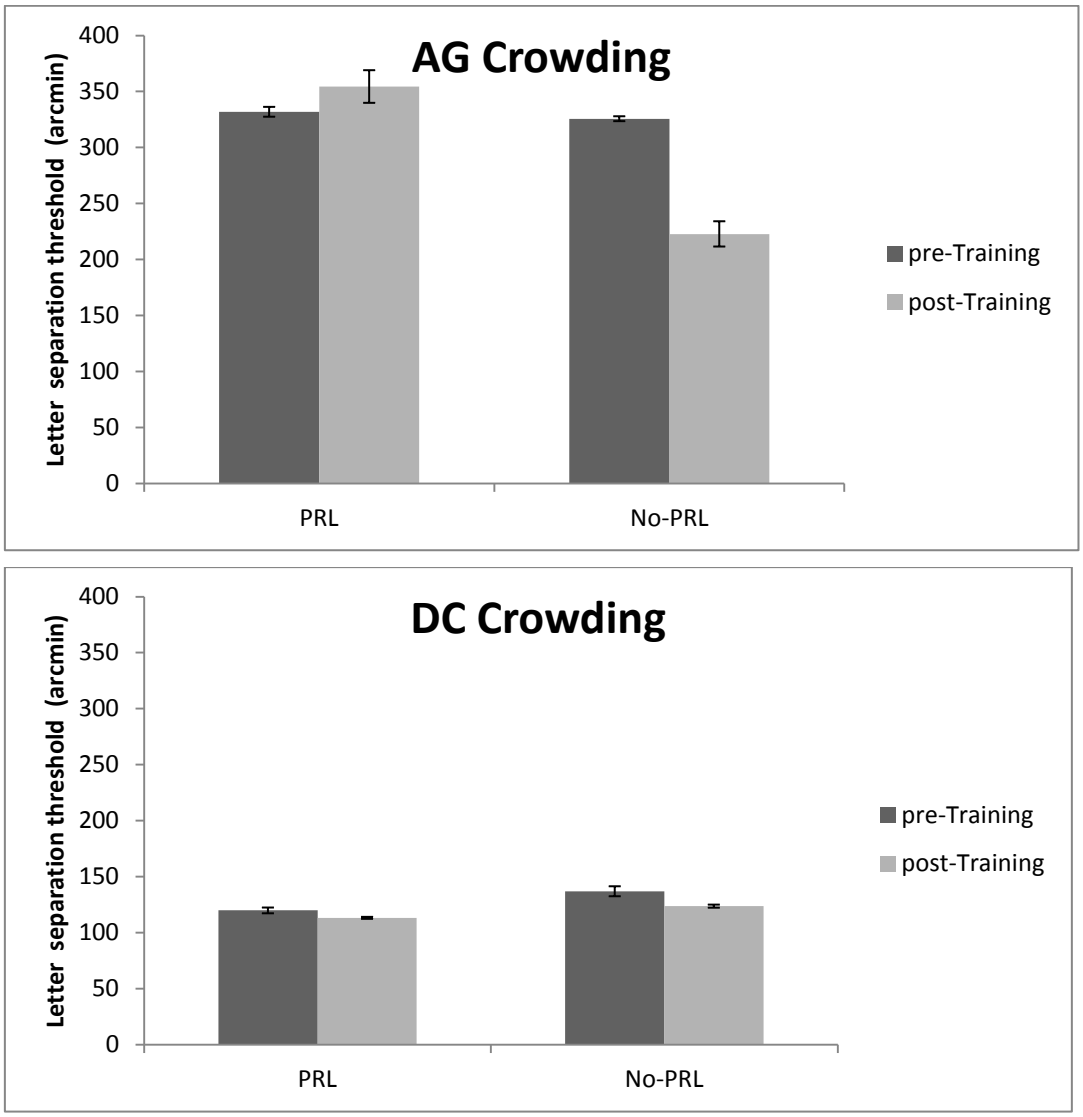


Figure 29: Critical space (crowding) thresholds before and after training for Maculopathy subjects. Error bars ± 1 s.e.m.

The training proven to be effective in crowding reduction for 2 of the 3 maculopathy subjects.

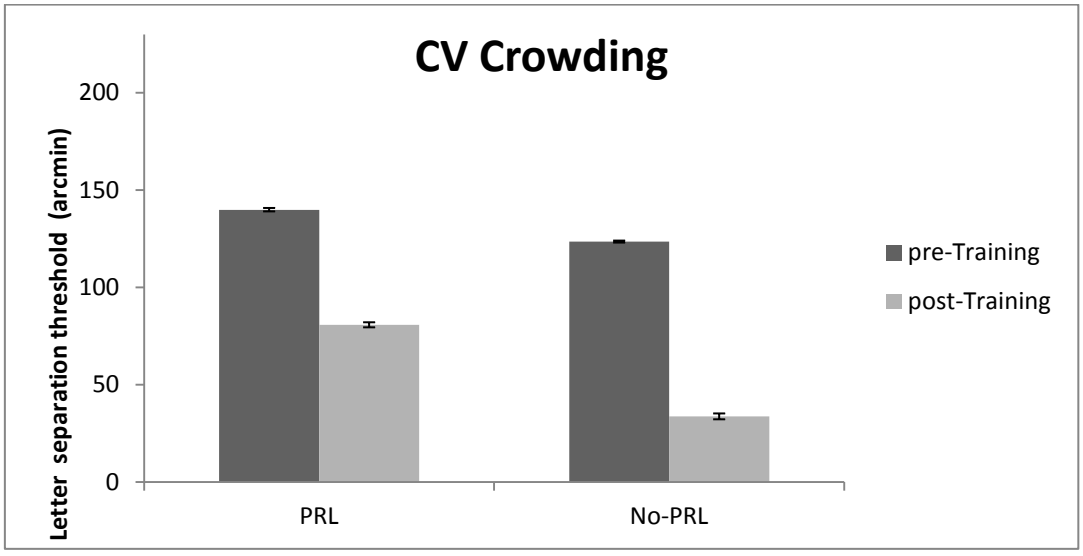
For subject MV, training did produce an apparent worsening of the performance. The explanation for this effect could be due to the fact that the subject had already very low critical spacing in the pre tests, even better than control subjects. So probably subject MV already reached the peak of improvement in crowding reduction due to a "natural training" before the pre tests. The results of subjects AG, showing an improvement for the No-PRL (supposedly less used, and consequently less "trained") but not for the PRL is consistent with this hypothesis.

Control Subjects

For CV, the training produced a crowding reduction in both retinal position (no-PRL: $t7 = 46.63$, $p < .0001$; PRL: $t7 = 8.716$, $p < .0001$).

For MM, a significant improvement was found for the PRL ($t7 = 118.18$, $p < .0001$) but not for the symmetrical retinal position, in which the post training performance was significantly worse (no-PRL: $t7 = 124.773$, $p < .001$;)

For MG, the training produced a crowding reduction in both retinal position (no-PRL: $t7 = 5.404$, $p < .0001$; PRL: $t7 = 21.726$, $p < .0001$).



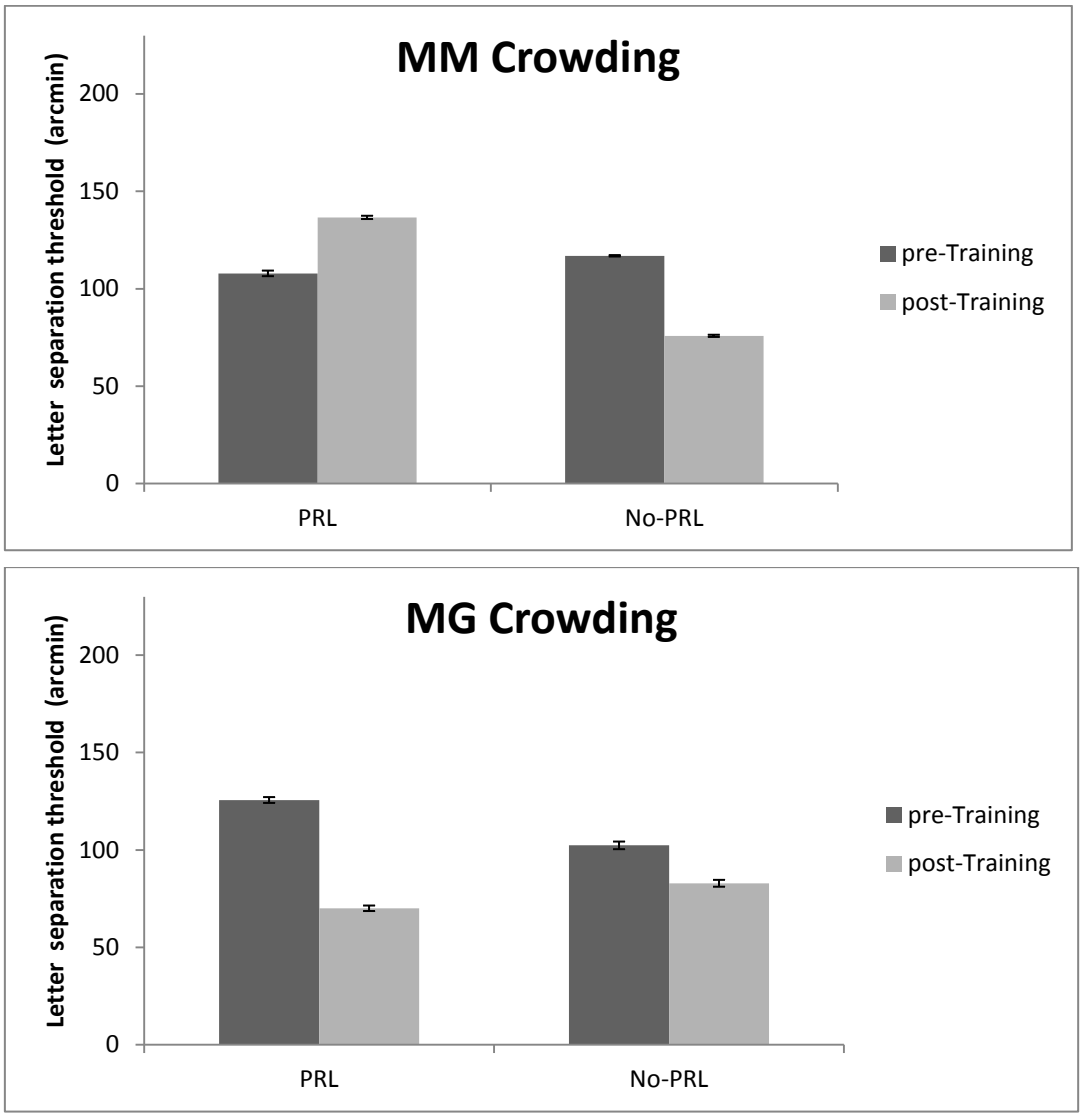


Figure 30: Critical space (crowding) thresholds before and after training for Control subjects. Error bars ± 1 s.e.m.

The results for the control subjects, showing a general reduction of crowding after training, are consistent with those reported from Experiment 1 and with the maculopathy patients (except for MM in the PRL position).

Transfer of learning to untrained eye

One of the interesting aspects of perceptual learning application to visual impairment treatments, such as the studies on amblyopia (Polat et al. 2004; Polat, 2009) is that, in some subjects, monocular training produced benefit also for the untrained eye (Polat et al., 2004; Polat, 2009).

The evidence that monocular training can produce a binocular benefit, as already proven with amblyopic patients, would constitute an important finding and improving the efficacy of a perceptual learning treatment for people with loss of central vision.

For one of the subjects, MV, and for the three control subjects, we were able to provide information about transfer of learning for Visual Acuity and Crowding measuring baseline and post training performance for the untrained eye.

Transfer of learning to VA (untrained eye)

Similarly to what we have done for the trained eye, we compared the last 8 reversals of the pre test measurements (3up/1 down Leavitt staircase) with the last 8 reversals of the post test, for the maculopathy subject and the three controls, individually.

Maculopathy Subject

For subject MV, training on contrast detection transfers to visual acuity both for PRL and no-PRL training sites(no-PRL: $t7 = 6$, $p < .001$; PRL: $t7 = 6.67$, $p < .0001$).

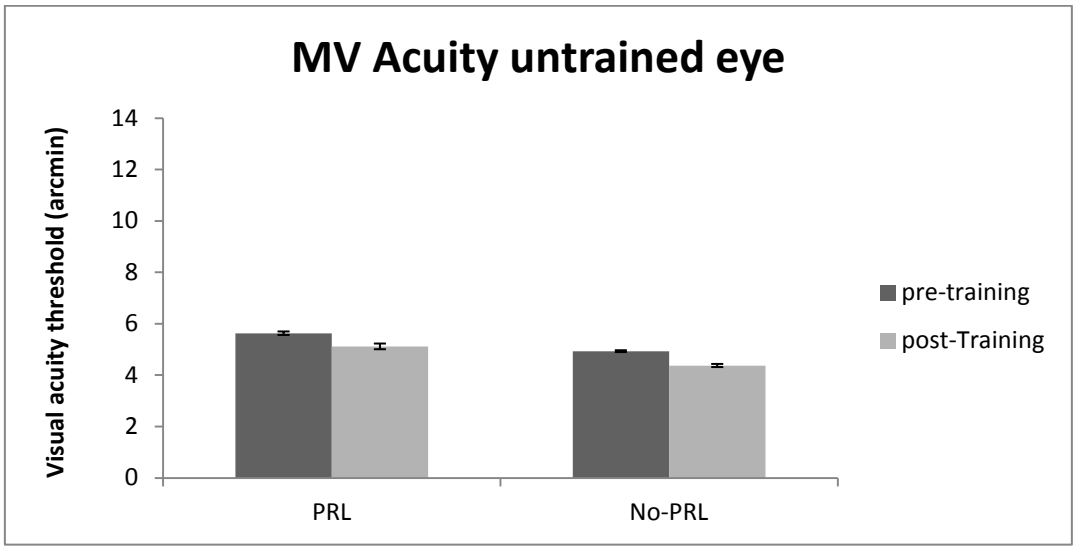


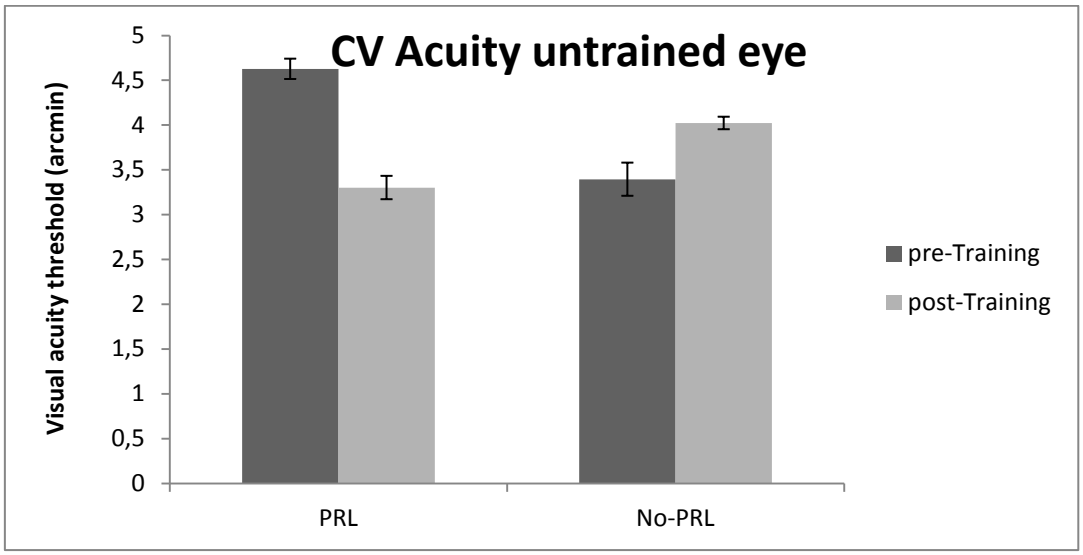
Figure 31: Visual Acuity thresholds before and after training for Maculopathy subject MV (untrained eye). Error bars ± 1 s.e.m.

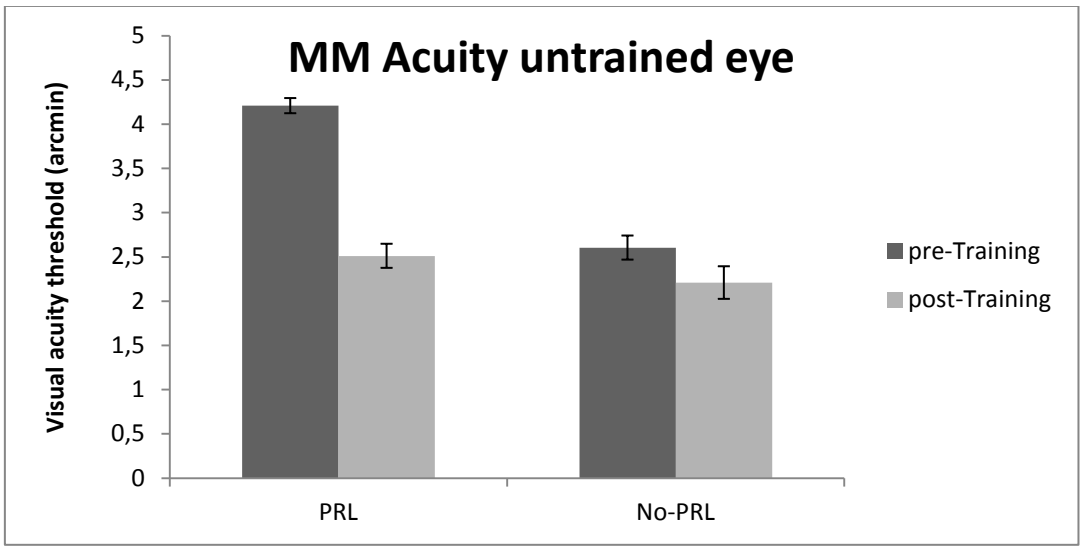
Control Subjects

For subject CV, training on contrast detection transferred to visual acuity for PRL (t_7 = 20.35, $p < .001$) but worsened the performance in the No-PRLsite (t_7 = 3.112, p = .017).

For subject MM, training on contrast detection transferred to visual acuity both for PRL and no-PRL training sites (PRL: t_7 = 10.681, $p< .0001$; no-PRL: t_7 = 5.388 , $p < .001$).

For subject MG, training on contrast detection worsened the visual acuity for no-PRL (t_7 = 2.758 , p =.028), while for the PRL there was no change in performance (t_7 = 1.457, p = 0.118)


CV Acuity untrained eye
Visual acuity threshold (arcmin)
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5
0
PRL
No-PRL
pre-Training
post-Training


MM Acuity untrained eye
Visual acuity threshold (arcmin)
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5
0
PRL
No-PRL
pre-Training
post-Training

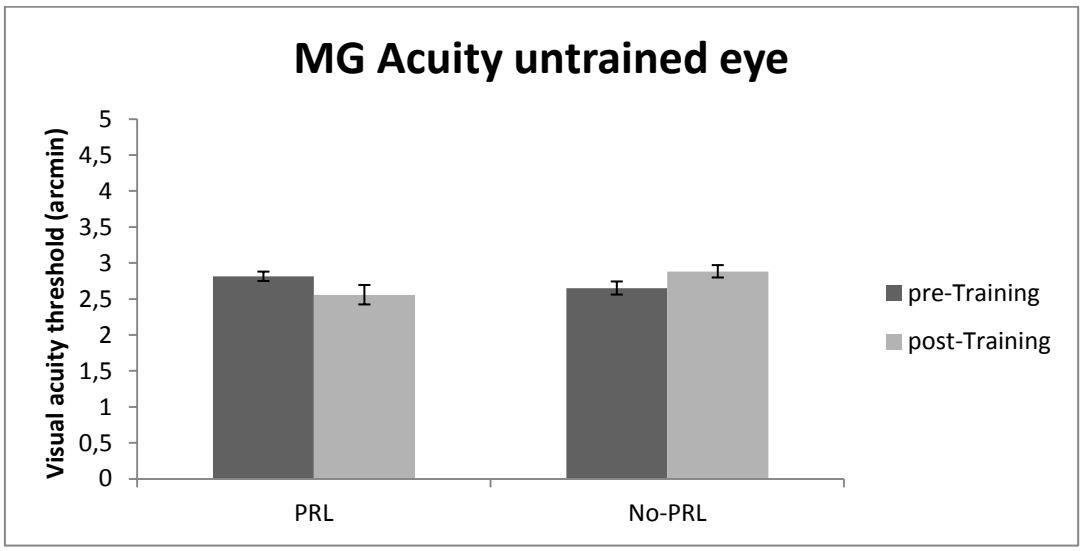

MG Acuity untrained eye
Visual acuity threshold (arcmin)
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5
0
PRL
No-PRL
pre-Training
post-Training

Figure 32: Visual Acuity thresholds before and after training for Control subjects (untrained eye). Error bars ± 1 s.e.m.

Transfer of learning to CW (untrained eye)

As before, we compared the last 8 reversals of the pre test measurements (3up/1 down Leavitt staircase) with the last 8 reversals of the post test, individually for each subject.

Maculopathy Subject

For subject MV, training on contrast detection did not result in a crowding reduction in the untrained eye, but in an increase of critical space for both for PRL and no-PRL training sites (no-PRL: $t7 = 39.6$, $p < .0001$; PRL: $t7 = 145.115$, $p < .0001$).

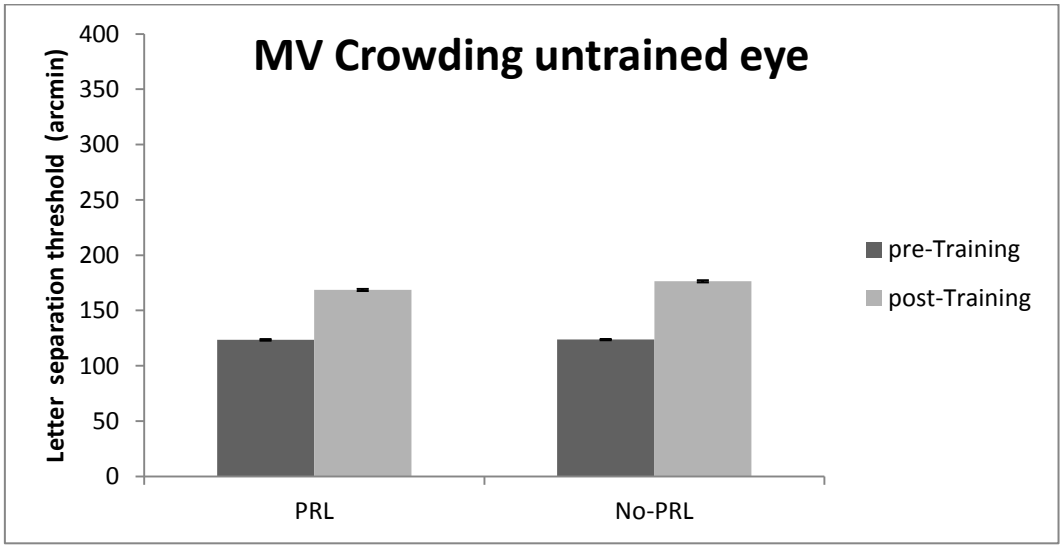


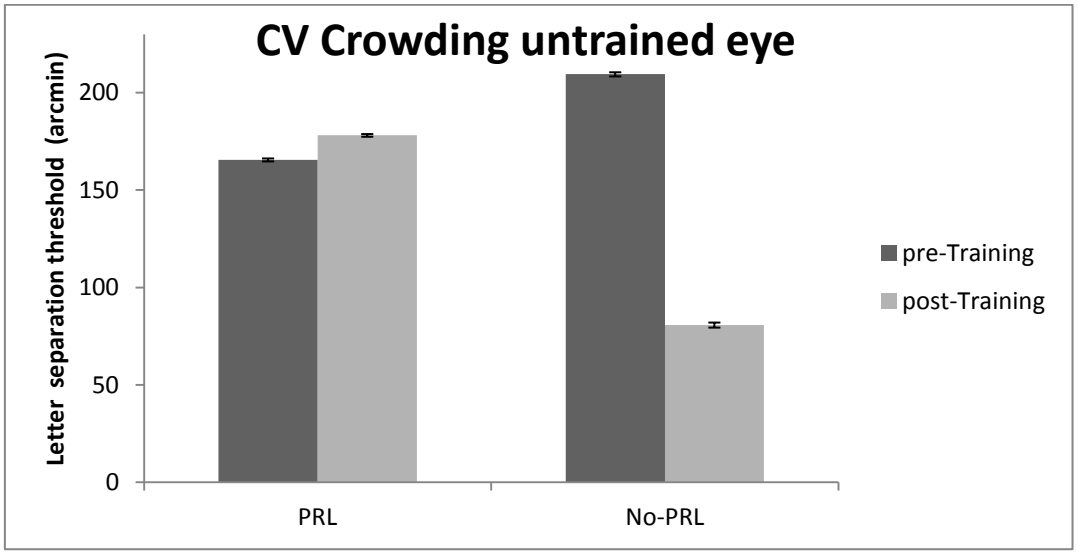
Figure 33: Critical space (crowding) thresholds before and after training for Maculopathy subjects. Error bars ± 1 s.e.m.

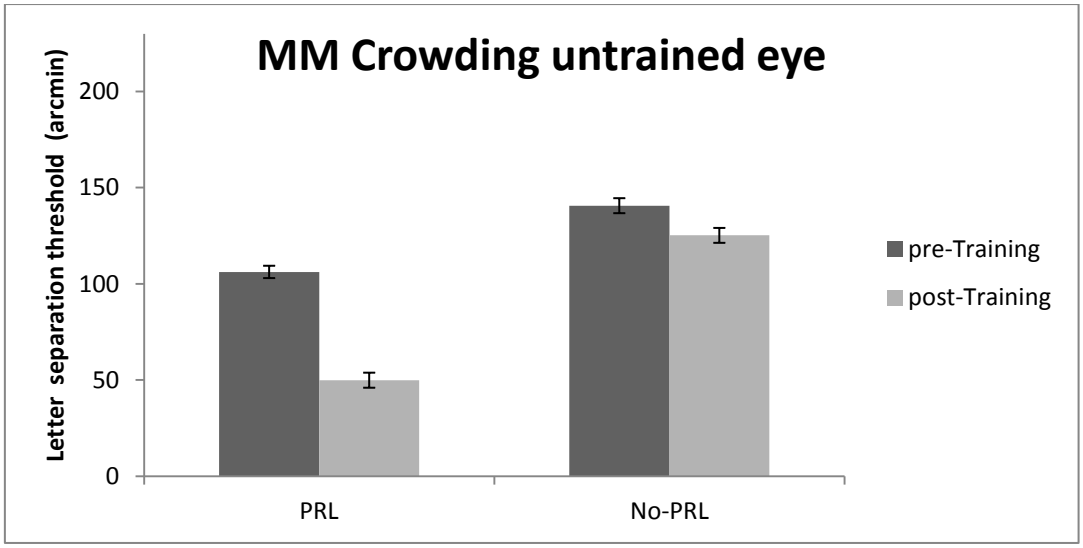
Control Subjects

For CV, the training produced in the untrained eye a crowding reduction in the No-PRL location (: $t7 = 57.591$, $p < .001$), while in the PRL produced a significant increase in critical spacing ($t7 = 20.454$, $p < .0001$).

For MM, a significant improvement in the untrained eye was found for both PRL ($t7 = 14.951$, $p < .0001$) and No-PRL ($t7 = 3.437$, $p = .011$;)

For MG, the training produced in the untrained eye an increase of critical spacing for both retinal position (no-PRL: $t7 = 3.802$, $p < .0001$; PRL: $t7 = 48.661$, $p < .0001$).





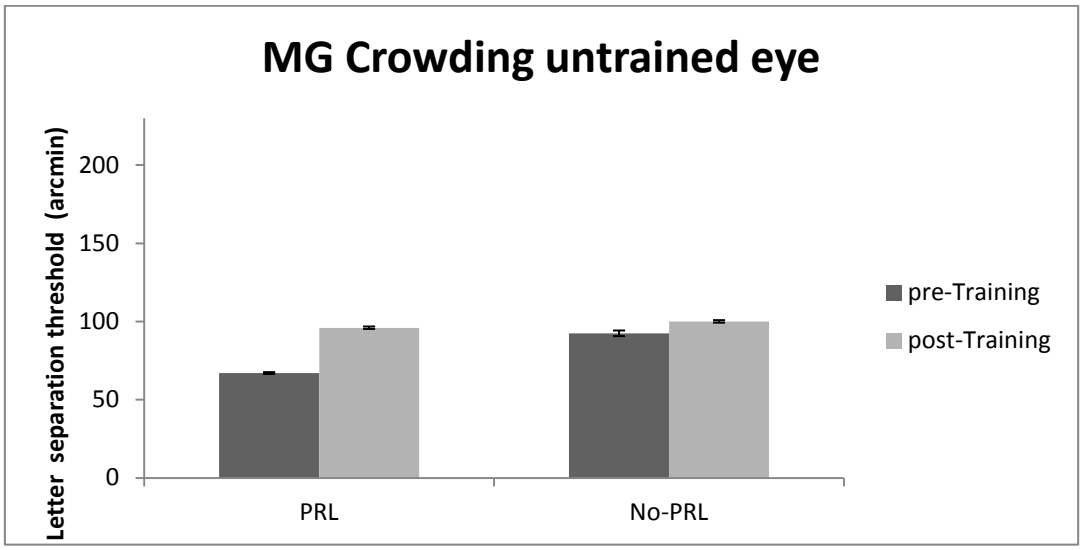


Figure 34: Critical space (crowding) thresholds before and after training for Control subjects. Error bars ± 1 s.e.m.

As for the transfer to crowding in the trained eye discussed earlier, in the untrained eye the pattern of results for the maculopathy subject seems consistent: patient MV showed an increase of critical spacing for crowding. For control subjects, results are less consistent, with one subject (CV) showing a significant reduction for one of the spatial positions but an increase for the other; another subject (MM) reporting improvement in performance for both positions, and another (MG) showing a worsening in performance for both PRL and No-PRL. Overall, our data do not support a transfer of learning to crowding reduction.

Discussion

The aim of Experiment 3 was to investigate lateral interactions at the periphery of the visual field in maculopathy patients (and control subjects) and verify whether a perceptual learning treatment would produce an improvement in the trained task that transfers to other, untrained, visual abilities.

On the basis of the results of Experiment 1, in which we reported the efficacy of a peripheral perceptual learning paradigm applied to lateral interactions, we modified the

training display in order to improve the effect of the training by reducing spatial uncertainty. As previous studies reported, collinear facilitation is influenced by attention (Freeman et al., 2001) and differences in allocation of attention could produce different pattern of lateral modulations at the periphery of the visual field (Shani and Sagi, 2005). As a consequence, we tested and trained both group of subjects (maculopathy and control) by keeping the stimuli configuration in the same retinal location throughout the training. In absence of eye tracking, the short presentation of 133 ms for each trial prevented subject from eye movements effect. Unfortunately, the procedure used (3 up/1 down staircase with yes/no paradigm) resulted in unreliable thresholds for contrast detection, leading us to use a detection sensitivity measure (d-prime), discarding the orthogonal threshold and consequently losing information about the architecture of peripheral lateral interactions in the maculopathy subjects. In fact, as Shani and Sagi (2005) reported, confuting the finding of Giorgi et al. (2004), peripheral collinear facilitation can only measured by comparing thresholds for collinearly and orthogonally flanked targets. In general, considering the pre test performance, there seems to be an increase in detection sensitivity with increasing the target-to-flanker separation, but we cannot make inference about whether this is an indication for collinear facilitation in maculopathy subjects. However, lateral masking curves seem not to differ consistently between maculopathy and control subjects. Training produced an increase in d-prime values that in the maculopathy subjects was more pronounced for medium and large target-to-flankers separations, while for control subjects, consistently with Experiment 1, the effects of training appear stronger for shorter separation.

Training effects transfer effectively to visual acuity in both maculopathy subjects and control subjects. The latter evidence is a new result respect to Experiment1, in which perceptual learning transferred only at crowding reduction. We argued that the reason was that, at least in the first stages, crowding and surround suppression share the same filters, or, according to an hypothesis recently reported by Lev and Polat (2011), that crowding and lateral masking at the periphery could be influenced by lateral interactions in a similar way. The hypothesis regarding the absence of transfer to visual acuity claimed the need for a more differentiated training, involving different orientations, since visual acuity, in our experiments and also as a standard practice, is measured by using alphabetical letters, that are composed by bars with different orientations. On the

other hand, in Experiment 1 the attention of the subjects was necessarily diffuse, since the target could appear either at the left or at the right of the fixation spot, for a total of 8° of visual angle of distance between the two spots in which the target could appear. In Experiment 1, target appeared only in one location, allowing subjects to focus their attention to just one visual region. Since allocation of attention seems to be one of the more evident difference between foveal and peripheral vision, (that is, attention in the periphery is reduced and more influenced by individual differences) the reduction of the space that subjects had to attend could have beneficially improved their ability to focus. Moreover, Freeman et al. (2001), showed that lateral interactions are influenced by attention (even though, in that case attention was focused on a feature – orientation, not just to a spatial position). In Experiment 3 we just reduced the visual space to attend. Moreover, by forcing subjects to attend a portion of the visual field, training could have improved their fixations, that before training, was diagnosed as unstable for all the maculopathy subjects. Also, the use of monocular vision could have further increase focusing and led to a more effective improvement after training (see Chapter 2 for a distinction between training with focused attention and training with distributed attention). What is interesting to notice, looking at the baseline performance of the maculopathy subjects (pre-training), is that visual acuity in all the three subjects was better in the no-PRL. This evidence is consistent with the hypothesis of Dilks et al. (2009), that cortical reorganization is not driven by specific factors but rather is a product of habit. Moreover, the evidence that in maculopathy subject AG training did not transfer to crowding in the PRL but it did for No-PRL, is a further evidence for a user-dependence of the PRL. In general, the results of crowding are different for the two groups: while for control subjects there is a overall confirmation of the results of Experiment 1 (reduction of crowding after training), 2 of the 3 maculopathy patients did not show improvement in critical spacing. In Chapter 2, we discussed about the limits of what can be learned and consequently improved, and the periphery of the visual field presents anatomical constraints that cannot allow improvements more than a certain level. Since these subjects are forced to use the periphery of the visual field to perform complex visual task, they could have "naturally trained" the periphery, so that it already reached the maximum performance. According to this hypothesis, the results of crowding increase for subject MV could be considered a "roof effect". An evidence for

this hypothesis comes from the comparison between baseline performances of subject MV and control subjects, showing that the thresholds for crowding are similar or even better than controls.

The results of AG are more clearly in the direction of natural training for the crowding: training resulted in a reduction of critical space for the No-PRL, the retinal region usually not naturally used, but had no effect on the PRL site. Moreover, the critical space of AG was the highest out of all the three maculopathy subjects. Since MV was the youngest of the three maculopathy patients, it could be possible that its neural plasticity reached its peak faster than the other two subjects (i.e. before the training), so the training, at least for crowding, had little effect. The absence of improvement in the Contrast Sensitivity Function is more likely to be due to the small sample, since the method used, differently from the Visual Acuity and the Crowding measurements, did not allow us to compare pre and post performances individually for each subjects. In any case, as Polat (2009) reported, improvement in the contrast sensitivity functions are crucial for the transfer of improvement to higher level functions, since these higher level functions rely on the input coming from the units at the early stages of visual analysis that respond to contrast differences. Moreover, consistently with the finding of Polat et al. (2004) with amblyopic patients, monocular training transferred to untrained visual abilities to the untrained eye. This is an important evidence since often in the maculopathy patients the scotoma is present in both eyes, so differently from amblyopia, there is not a natural compensation between the two eyes. A bigger sample is probably needed to generalize this statement, but from the one maculopathy subject who performed pre and post tests on the untrained eye, it seem that a binocular benefit could be obtained out of a monocular training. Taken together, this results indicate that perceptual learning can improve peripheral visual functions in clinical subjects with loss of central vision, as already proven for foveal vision (Polat et al., 2004; Polat, 2009; Tan and Fong, 2008). Moreover, improvement of peripheral visual abilities is not a result confined to the area of clinical treatment: also for normal sighted subjects, peripheral vision is important in tasks such as mobility (Nakayama 1985; Geruschat and Smith 1997; Geruschat, Turano and Stahl, 1998; Greer; 2004; Kuyk, Elliott and Fuhr, 1998; Marron and Bailey, 1982; Noe, Ferraro, Lamaoureux, Rait and Keefe, 2003; Rieser, Hill, Talor, Bradfield and Rosen, 1992; Turano, Broman, Bandeen-Roche, Munoz and

Rubin, 2004; Turano, Rubin and Quigley, 1999; Vargas-Martin and Peli 2006). Moreover, reduced visual fields negatively affect visual-motor performances, such as postural stability (Black, Wood, Lovie-Kitchin and Newman, 2008; Shabana, Cornilleau-Peres, Droulez, Goh, Lee and Chew, 2005; Turano, Herdman and Dagnelie, 1993; Turano, Dagnelie and Herdman, 1996), locomotion (Marigold, 2008), driving (Bowers, Peli, Elgin, McGwin and Owsley, 2005). Experimental studies (Ball, Owsley, and Beard, 1990; Ball and Owsley, 1993) showed that the use of peripheral vision is subject to individual differences: estimations of ‘‘useful field of view’’ decrease with age also in non pathological conditions. This reduction of use of peripheral vision has been found to predict risks of car crashes in elderly drivers (Clay, Wadley, Edwards, Roth, Roenker and Ball, 2005; Owsley, Ball and McGwin, 1998). Therefore, peripheral vision improvements could be useful also for normal-sighted people.

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Chapter 6

Experiment 4: Peripheral Lateral Interactions in a Maculopathy patient: a different procedure

The aim of Experiment 4 was to investigate lateral interactions in the periphery of the visual field in maculopathy subjects, but adopting a different procedure for the measurement of contrast thresholds respect to the one used in Experiment 1 and 3. In Experiment 3, one of the main problems concerned post test contrast thresholds measurements. Maculopathy subjects, probably as a consequence of their unstable fixation (that characterize our subjects and maculopathy patients in general), produced a high number of FA that in a yes/no procedure applied to a 3up/ 1 down staircase (Levitt, 1971), resulting in unreliable thresholds. Whereas in Experiment 1, the identical yes/no procedure adopted for pre and post test thresholds measurement proven to be reliable when compared with d prime obtained from the first and last week of training (Figure 6 and 7), in Experiment 3 this led us to discard pre and post test contrast thresholds and to analyze only d primes from the first and last week of training, losing in turn information about orthogonal thresholds and consequently about the architecture of lateral interactions in the periphery of the visual field in maculopathy subjects. In any case, Acuity and crowding measures, being conducted with a discrimination task, were not subjects to response bias, so the transfer results reported in Experiment 3 are reliable.

Moreover, while simulation studies showed that the threshold estimations obtained from two-alternative forced-choice (2-AFC) paradigm are less efficient respect to a yes/no paradigm, using the same number of trials (Alcalà-Quintana and Garcìa Pèrez, 2004b, Garcìa-Pèrez, 1998, 2001; Garcìa-Pèrez and Alcalà-Quintana, 2005; Kershaw, 1985; Taylor and Creelman, 1967), it has been noted that yes/no procedure is subject to response bias and criterion shifts (Green and Swets, 1974).

In order to avoid false alarms in the new set of tests, and producing a more reliable estimation of thresholds, we adopted a temporal 2AFC procedure.

The method to use in order to uncover collinear lateral interactions at the periphery of the visual field has been a topic of discussion among visual scientists: Giorgi, Soong, Woods and Peli (2004) reported that a temporal 2AFC allowed to measure collinear lateral interactions at the periphery, whereas spatial 2AFC and yes/no procedure did not. On the other hand, Shani and Sagi (2005) reported that neither a temporal nor a spatial 2AFC procedure (Williams and Hess, 1998; Zenger-Landolt and Koch, 2001) were able to spot collinear facilitation at the periphery when comparing orthogonal and collinear flankers. In Experiment 1, we were able to find consistent collinear facilitation with a yes/no procedure, in agreement with recent findings (Lev and Polat, 2011).

The change of procedure, in Experiment 4, is therefore mainly driven by the idea that maculopathy subjects could experience more difficulty in a paradigm subject to bias.

Consequently, in Experiment 4, rather than focusing on the effects of training (already proven to be effective in transferring to other, untrained visual abilities both in normal subjects and in maculopathy patients), we were interesting in investigating the architecture of lateral interactions in the periphery of the visual field of maculopathy patients and whether perceptual learning is effective in modulating them.

Moreover, we tested a group of control subjects in order to verify consistency between yes/no and temporal 2AFC measurements. Since we assumed that, at least in normal-sighted people, two symmetrical locations in the periphery of the visual field are structurally homogeneous, in Experiment 4 we tested control subjects presenting stimuli configuration always in the same retinal position.

Method

Apparatus

Stimuli were displayed on a 19-inch Asus ML228 LCD monitor with a refresh rate of 75 Hz. The flankers and target stimuli, as well as the CW stimuli, were generated with the Matlab Psychtoolbox (Pelli, 1997; Brainard, 1997). The screen resolution was 1280 x 1024 pixels. Each pixel subtended ~1.9 arcmin. We used a gamma-corrected lookup table (LUT) so that luminance was a linear function of the digital representation of the image.

Subjects

One maculopathy patient, FM, and three normal-sighted subjects who were unaware of the purpose of the study participated in the experiments.

Subject FM (51 years old at the time of testing) was diagnosed with essudative maculopathy and presented a central scotoma of ~ 6 deg in the left eye.

Location of the stimuli

As for the maculopathy subjects involved in Experiment 3, for maculopathy subject FM we measured the dimension of the scotoma and the position of the PRL respect to the center of the retina. According to these measurements, PRL was located at 2.88 deg above and 3.2 deg at the left of the fixation point, whereas No-PRL was located at 2.88 deg below and 3.2 at the left of the fixation point.

Stimuli

Stimuli were Gabor patches consisting of a cosinusoidal carrier enveloped by a stationary Gaussian. The mean luminance of the display was 46.7 cd/m_2. Each Gabor patch was characterized by the sinusoidal wavelength λ, phase φ, and SD of the luminance Gaussian envelope (σ) in the (x, y) space of the image:

$$G(x, y) = \cos(2\pi / \lambda x + \varphi) \exp(-(x^2 + y^2) / \sigma^2) \qquad \text{Eq.1}$$

In all experiments, $\sigma = \lambda$ and $\varphi = 0$ (even symmetric). Gabors had a spatial frequency of 1 cpd. For the maculopathy subject FM, the location of the target relative to the fixation point (0.18 deg) was in the point of the visual field corresponding to the Preferential Retinal Locus PRL) and in a symmetrical locus ("No-PRL"), varying between blocks. For normal-sighted subjects, the location of the configurations was at 4 deg up and 4 deg left respect to the fixation point. In each session the position of the configuration was always the same (i.e. PRL or No-PRL). As for all the other Experiments, a vertical Gabor target was presented flanked, above and below, by two high-contrast Gabor patches (0.6 Michelson contrast). During the tests and the training, the flankers were

always vertically oriented and located at various distances from the target (i.e., 2λ, 3λ, 4λ, and 8λ). The tests were conducted monocularly, with control subjects using the non-dominant eye and maculopathy subject using the eye with the scotoma.

Procedure

Lateral interactions were tested by comparing the contrast detection of a vertical Gabor target (1 cpd) flanked by either two vertically oriented Gabor patches (collinear condition – Fig. 12A) or two horizontal Gabors (orthogonal condition – Fig. 12B) with target-to-flankers distances of 2λ, 3λ, 4λ, and 8λ. The contrast detection threshold was measured for the target Gabor presented at the PRL and at the No-PRL for the maculopathy subject FM, whereas control subjects attended a configuration that appeared 4 deg above and 4 deg at the left of the fixation point. Each stimulus was presented for 133 ms. For the maculopathy subject, each training sessions consisted in 8 blocks, with different target-to-flankers separation and spatial position, starting from the highest distance (8λ) with presentation in the PRL and in the No-PRL in separate blocks. For the control subjects, each sessions was composed by 4 blocks, one for each target-to-flankers separation, starting from the largest separation (8λ). Training was carried on for 8 weeks, with 3 weekly session each. The procedure adopted was a temporal 2AFC, with the subjects presented with two intervals, one containing the flankers with the target and the other containing only the flankers. Each session ended after 120 trials or 16 reversals, with the thresholds measured as the average value of the last 8 reversals. The 3 up/1 down staircase allowed us to measure a threshold corresponding to 79% of correct detection for the central target.
Statistical comparisons were conducted using Student's t-tests.

Results

Lateral interactions curves

Maculopathy subject

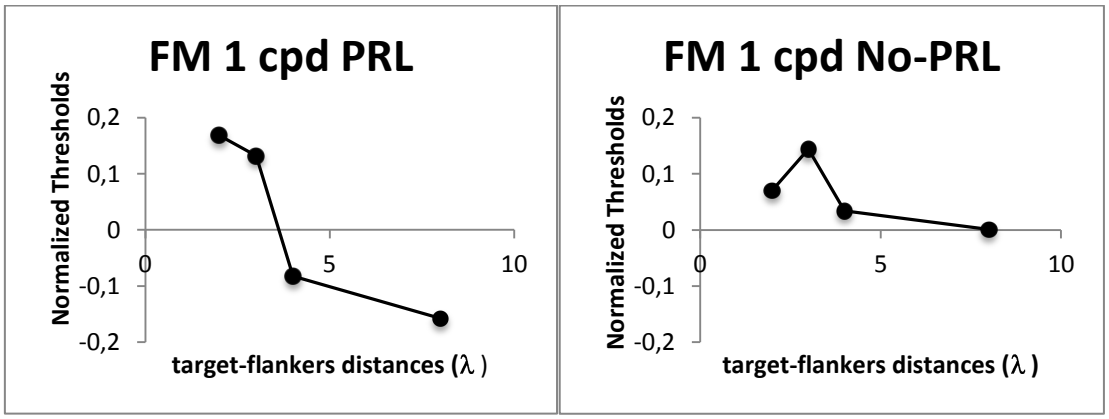

Figure 35: lateral interaction curves for maculopathy subject FM, for presentation of a target vertically flanked at the PRL (left) and in a symmetrical retinal position (No-PRL, right). Normalized thresholds are obtained by comparing orthogonal and collinear thresholds: when the values are below the zero, there is facilitation, whereas when values are above zero, there is collinear inhibition.

Interestingly, lateral interactions curves, in the maculopathy subject (showed in figure as the normalized thresholds between orthogonal and collinear thresholds, with values below zero indicating facilitation and values above zero indicating collinear inhibition), differ between PRL and No-PRL. In the PRL condition, maculopathy subject FM showed collinear facilitation at 8 λ (t_2=11.057, p = .008), consistently with the data for normal-sighted subjects reported in Experiment 1, but he reported lower thresholds for the collinear condition (respect to rthogonal) at 4 λ of target-to-flankers distance as well (t_2=4.373, p = .049), indicating collinear facilitation. On the other hand, in the No-PRL condition, subject FM did not show collinear facilitation for 8λ nor for 4λ.

Control subjects

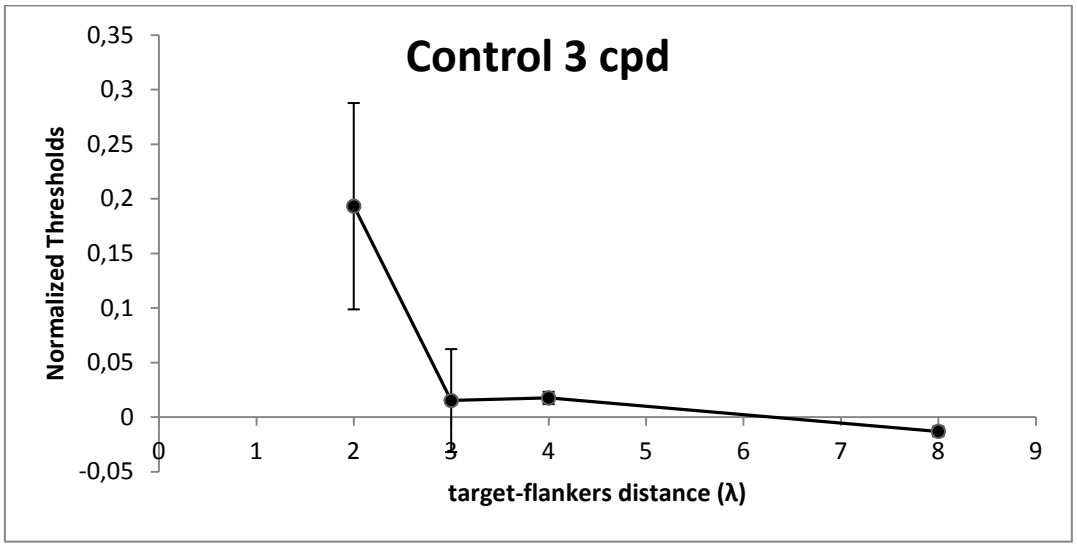

Figure 36: lateral interaction curves for control subjects, for presentation of a target vertically flanked at the PRL (left) and in a symmetrical retinal position (No-PRL, right). Normalized thresholds are obtained by comparing orthogonal and collinear thresholds: when the values are below the zero, there is facilitation, whereas when values are above zero, there is collinear inhibition.

Lateral Interaction curves in the control subjects resemble the ones reported in Experiment 1, with collinear thresholds lower than the orthogonal (values below zero in the normalized thresholds) for the larger separation tested (8λ). However, due probably to the small sample, the collinear facilitation at 8λ is not statistically significant.

Perceptual Learning

Maculopathy subject

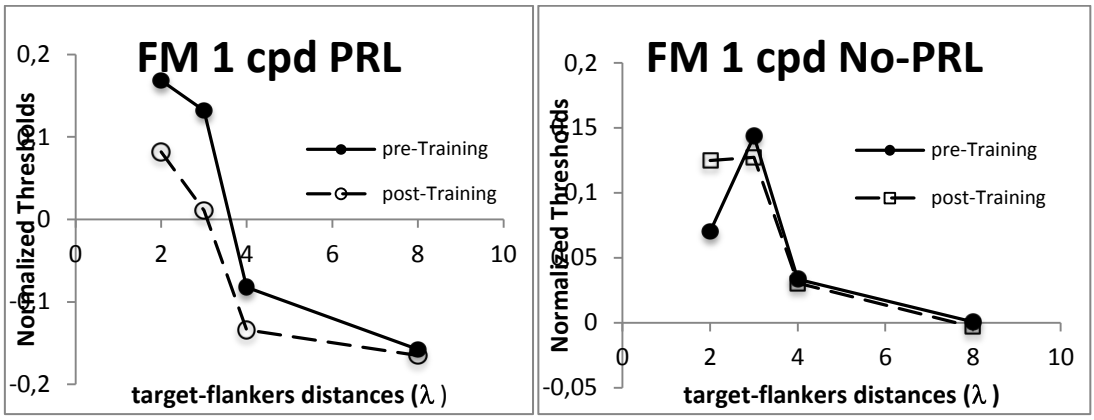

Figure 37: lateral interaction curves for maculopathy subject FM, before and after training, for presentation of a target vertically flanked at the PRL (left) and in a symmetrical retinal position (No-PRL, right). Normalized thresholds are obtained by comparing orthogonal and collinear thresholds: when the values are below the zero, there is facilitation, whereas when values are above zero, there is collinear inhibition.

For maculopathy subject FM, training in the PRL appears to have reduced thresholds for the shorter and medium target-to-flankers distances, with the collinear threshold for 3 lambdas separation almost reaching the value of the orthogonal condition. However, training on the No-PRL seems to not have almost no effect in modulating lateral interactions.

Control subjects

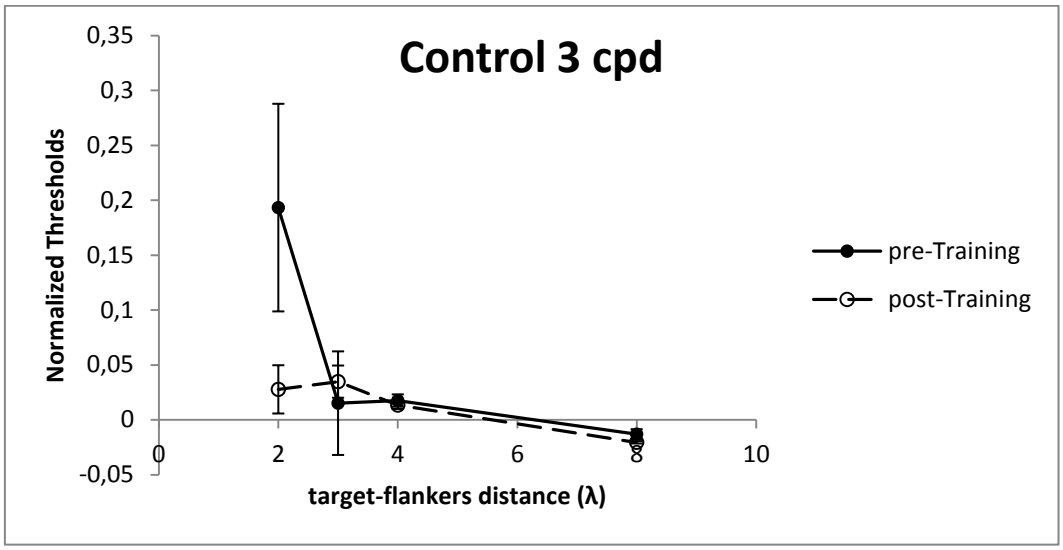

Figure 38: lateral interaction curves for control subjects, before and after training, for presentation of a target vertically flanked at the PRL (left) and in a symmetrical retinal position (No-PRL, right). Normalized thresholds are obtained by comparing orthogonal and collinear thresholds: when the values are below the zero, there is facilitation, whereas when values are above zero, there is collinear inhibition.

For control subjects, training seems more effective in reducing inhibitory collinear interactions at the shorter target-to-flankers distances, consistently with Experiment 1.

Discussion

In Experiment 4, we aimed at studying the architecture of peripheral lateral interactions in a maculopathy subject. Since in Experiment 3 the three maculopathy subjects did not produce reliable thresholds for the lateral interactions sessions, here we adopted a different procedure.

Giorgi et al. (2004), reported that the right method is crucial in finding collinear facilitation, while we showed, in Experiment 1 and Experiment 4 that, at least for normal-sighted subjects, collinear facilitation can be reported with different paradigms. Moreover, while Giorgi et al. (2004) suggested that the ideal procedure would be a temporal 2AFC, Lev and Polat (2011) proposed a yes/no procedure as a more appropriate method. One of the reasons why Lev and Polat (2011) suggested that 2AFC is less reliable in measuring peripheral lateral interactions is that it can produce fatigue

in the subjects and thus disturb the stability of the fixation. However, with maculopathy subjects, known to have an unstable fixation, we found a more reliable measurements and thresholds estimation with a 2AFC procedure, that avoided false alarms. The lateral interaction curve of the maculopathy subject FM is consistent with the d-prime measurements of Experiment 3: while in Experiment 3 detection sensitivity increased with the target-to-flankers separation, in Experiment 4 collinear inhibition decreased, turning into facilitation for the two largest distance tested (4λ and 8λ). However, this pattern of results does not seem consistent between PRL and No-PRL, whereas in Experiment 3, d-prime did not seem to differ much between these two retinal locations. The different results between PRL and No-PRL in maculopathy subject FM can be due to the temporal 2AFC procedure used: while improving the overall reliability of the measurements, could have been more demanding when the presentation involved the No-PRL, a retinal locus these subjects are not used to visually attend with. This hypothesis is consistent with Lev and Polat (2011), suggesting that a yes/no procedure is less subject to drops of attention.

On the basis of the lateral interaction curve of subject FM, we can see that collinear facilitation in maculopathy patients can be seen already at 4λ of target-to-flankers separation, pointing in the direction of a cortical reorganization that, possibly via recruitment of cortical regions formerly representing the fovea, improved lateral interactions in the periphery of the visual field and spontaneously reduced the medium-range inhibition reported in control subjects and in previous studies (Shani and Sagi, 2005). Moreover, consistently with previous studies in fovea (Polat and Sagi, 1994b; Polat et al., 2004), and with the evidence of Experiment 1, in Experiment 4 we showed that lateral interactions in the periphery of the visual field of maculopathy patients can be modulated by perceptual learning, especially reducing the short-separation inhibition. However, this pattern of results seems clear for the training with stimuli presentation in the PRL, while for training in No-PRL, the lateral interaction curve does not appear modified. This results partially challenge the "use-dependent" hypothesis in the definition of the PRL, supported, among the others, by Dilks, Baker, Peli and Kanwisher (2009). Whereas lateral interactions curves in the pre-test could have resulted different because of a "use-dependent" reorganization, that produced a reduction of collinear inhibition already at 4λ in the PRL, the absence of training effects

on the No-PRL points in the direction of a structural difference between these two retinal location. However, an alternative hypothesis involves the attention: since the PRL is the retinal locus on which these subjects spontaneously focus attention, the reduced attentional allocation in the No-PRL could have negatively affected the efficacy of the collinear configuration training, not fully probing collinear interactions, consistently with previous studies on attention and lateral interactions (Freeman, Sagi and Driver, 2001)

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Chapter 7

General Conclusion

As stated in the Introduction, the aim of this thesis was threefold: shed light on the collinear facilitation in the periphery of the visual field, that in previous studies resulted inconsistent, investigating the possibility of modulating peripheral lateral interaction through perceptual learning, and attempting to create a practical treatment for improving visual abilities of people affected by central vision loss.

Regarding the first point, while collinear interaction (the modulation of contrast thresholds produced by the presence of flanking elements) in the fovea is a strong and consistent phenomenon, with clear and constant boundaries between inhibitory area (target-to-flankers distances up to 2.5 times the size of the stimuli used, commonly Gabor signal) and excitatory area (target-to-flankers distances from 2.5 to 10 times the Gabor size, with the peak of facilitation when the distance is three times the stimulus size) previous studies on lateral interactions in the periphery of the visual field did not find consistent evidence for collinear facilitation. Williams and Hess, in 1998, tested subjects at 3° of eccentricity and only one of them reported facilitation at 6λ (6 times the size of the stimuli used), a larger separation than the one usually producing facilitation in fovea (3λ). In 2001, Zenger-Landolt and Polat did not find facilitation of subjects tested at 4λ. A previous study, by Polat and Sagi (1994b) did report facilitation, but only as a side-note, not showing any data. In 2004, Giorgi, Soong, Woods and Peli (2004) reported consistent collinear facilitation in the near-periphery, but, as pointed out by Shani and Sagi (2005), they probably did not use the proper method, since they compared collinear and no-flankers condition, without distinguish between collinear facilitation and reduction of spatial uncertainty. Shani and Sagi (2005) suggested that the right control for peripheral lateral interactions would be comparing contrast thresholds for the collinear and the orthogonal condition, allowing to separate collinear effect from "cueing" effect. Moreover, since previous studies (Freeman, Sagi and

Driver, 2001) showed that allocation of attention plays a crucial role in eliciting lateral interactions, Shani and Sagi (2005) used a dual task procedure in order to force subject to attend the peripheral flankers.

They reported that with the allocation of attention to the flankers, some subjects showed revealed collinear facilitation. In Experiment 1, we reported that collinear facilitation (respect to orthogonal condition, Shani and Sagi, 2005) is consistently present in the near-periphery of the visual field (4° of eccentricity), at a target-to-flankers separation larger than in fovea (8λ), consistently with the most recent study on peripheral collinear facilitation (Lev and Polat, 2011, reporting facilitation for separation of 7λ).

Regarding the second point, the effectiveness of perceptual learning in modulating lateral interactions in the periphery of the visual field, in Experiment 1 we showed that training is effective in producing modifications of lateral interactions and, most importantly, it produces a transfer of learning to higher-level, untrained functions as the reduction of crowding, the deleterious effect on stimulus discrimination by flanking elements. While this result is in contrast with previous report using a similar paradigm (Shani and Sagi, 2005), probably because the short period of training, is consistent with studies with foveal presentation of the stimuli, both in normal-sighted subjects (Polat and Sagi, 1994b) and in patients with blurred vision (Polat, Ma-Naim, Belkin and Sagi, 2004; Polat, 2009; Tan and Fong, 2008).The rationale is that higher-level visual abilities rely on low-level inputs, such as those coming from contrast sensitivity units, so improving the information at early stages of visual processing ameliorates in turn more complex visual functions, as suggested by Polat (2009).

In Experiment 2, we further investigated whether the improvement in crowding reduction reported in Experiment 1 is the product of perceptual learning at early stages of visual processing, pointing out the spatial and orientation selectivity of the contrast detection improvement in subjects trained on collinear configuration. Interestingly, we reported a reduction of contrast thresholds for the collinear condition despite the training was carried on only one target-to-flankers separation thus appartently in contrast with Polat and Sagi (1994b), that showed how training only few separations does not produce improvement in contrast detection for the trained configuration.

Regarding the third point, whether a perceptual learning paradigm could be used to improve peripheral visual abilities of subjects with loss of central vision (such as maculopahty patients) by probing peripheral lateral interactions, in Experiment 3 we trained a group of subjects with maculopathy and a group of normal-sighed subjects.

People affected by maculopathy, a pathological condition of the macula, the central part of the retina, are forced to use a peripheral retinal location as the new fixation point (PRL, preferential retinal locus). In order to improve the efficacy of the training, and to test hypothesis regarding the functional specificity of the PRL respect to other peripheral retinal loci, we trained two different retinal position in separate blocks.

While in Experiment 1 the training configuration could appear either at the left or at the right of the fixation point, in Experiment 3 we presented the stimuli in two separate spatial locations, varying the position between blocks. Moreover, the training was conducted monocularly, in order to maximize the effect of the training. We showed that perceptual learning training is able to produce a significant increase in detection sensitivity for the trained configuration at the shortest target-to-flankers separation, both in normal and in maculopathy subjects. Moreover, we reported a transfer of learning to crowding reduction and visual acuity for normal-sighted subjects, while maculopathy subjects showed improved visual acuity but showed no effect on crowding. The improvement in visual acuity is a new result respect to Experiment 1, in which we found transfer of learning only to crowding reduction. One of the reasons could be the reduction of the visual space that subjects had to attend. The lack of consistent transfer to crowding reduction in maculopathy subjects could be attributed to a roof effect, since they showed, in the pre test performances, low crowding thresholds, so therefore they might have already "naturally" trained this visual ability in everyday life. Interestingly, we did not find huge differences between PRL and No-PRL neither in detection sensitivity nor in transfer effects. Moreover, we showed that monocular training transferred to the untrained eye for visual acuity, both for normal-sighted and maculopathy subjects. Thus, these data seem to indicate the concrete possibility of a binocular benefit out of a monocular training. In Experiment 4, we aimed at describing lateral interactions curves in a maculopathy subject. Since in Experiment 3 we were not able to draw conclusions on the architecture of lateral interactions due to the high number of false alarms, that in the staircase procedure with yes/no response produced

unreliable thresholds, we changed method adopting a temporal, two alternative forced choice (2AFC).

The right metodology to use in order to uncover lateral interactions in the periphery of the visual field has been object of discussion in previous studies: Williams and Hess (1998) and Zenger-Landolt and Polat (2001) used a spatial two alternative forced choice (spatial 2AFC) and did not find consistent collinear facilitation. Giorgi et al. (2004) suggested that a temporal 2AFC is the ideal procedure for investigating peripheral collinear facilitation, while Shani and Sagi (2005), with the same method, reported absence of consistent facilitation. More recently, Lev and Polat (2011) proposed a yes/no procedure, finding evidence for consistent facilitation at the periphery of the visual field, in agreement with our report in Experiment 1. In Experiment 4, we showed that the lateral interactions in the periphery of the visual field of the maculopathy subject could be facilitatory at shorter target-to-flankers distances (4λ) respect to normal-sighted subjects (8λ). Interestingly, this was true for PRL but not for the No-PRL, in which the maculopathy subject did not show collinear facilitation even for the largest distance tested (8λ). differently from normal-sighted subjects. Moreover, training resulted effective in modulating collinear lateral interactions in the PRL but not in the No-PRL, partially questioning the hypothesis of a "use-dependent" reorganization (Dilks, Baker, and Peli, 2009). Moreover, control subjects tested with the 2AFC procedure showed lateral interactions curves similar to the one reported for normal-sighted subjects in Experiment 1, showing that lateral interactions at the periphery of the visual field are at least partially independent from the method adopted.

Taken together, the results of this thesis produced reliable answers to the initial questions, showing the existence of consistent lateral interactions in the peripheery of the visual field for both normal-sighted and maculopathy subjects, and the efficacy of a perceptual learning paradigm that, probing these collinear interactions, is effective in improving higher-level, untrained visual abilities.

Future perspectives

As stated earlier, the application of perceptual learning pardigm for the treatment of visual deaseases is quite a recent accomplishment. Regarding maculopathy, and in general pathology concerning the loss of central vision, the studies here presented appear to be, to our knowledge, the first to investigate the possibility of improving the residual vision in these type of patients. Since pereptual learning is based on long-lasting changes in neronal network, and on the promotion of neuronal plasticity, it is very likely that in this type of individuals, in which regions of the retina are damaged but the cortical areas formerly representing the fovea are still intact, there are possibilities for neuronal reorganization even higher respect to other visual patlogy or defects treated with perceptual learning of lateral interactions, such as ambylopia, myopia and presbyopia. Future studies could take into account the possibility of integrate perceptual learning with techinques of brain stimulation, such as TMS (Transcranial Magnetic Stimulation) and tDCS (Transcranial Direct Current Stimulation). Indeed, a recent paper by Fertonani, Pirulli and Miniussi (2011), showed the possibility of inducing neural palaticity in the visual cortex by using tDCS, even though it was tested just between session, so no data have still been reported concerning long lasting change in neuronal network after transcranial stimulation, nor with the concomitant use of a lateral interaction training. On the basis of this evidence, there are interesting possibilities for combining recent techinques in order to develop a structured protocol of intervention and an effective treatment for these type of patients. Moreover, recent findings showed how improving peripheral vision could be benefical also for normal-sighted people, due to its involvement in everyday taks such as postural stability, locomotion and driving: indeed reduced use of peripheral vision has been found to predict risk of car crash even in absence of any visual pathology.

Summary

One way in which peripheral vision may acquire the functional role of the fovea, a part of the retina preferentially used for complex visual tasks (such as reading and face recognition) is by modulating the strength of intracortical connections in the humans' visual areas with perceptual learning. Perceptual learning is a practice-dependent improvement in a visual task performance that can persist for several months, and is specific for stimulus, task, eye presentation and retinal locus of stimulation. These specificity effects have been explained on the basis of neural plasticity, consisting in long-term modifications of a number of mechanisms in the early visual cortices, that are selective for basic stimulus attributes (Karni & Sagi, 1991, 1993; Ahissar & Hochstein, 1993, 1996; Casco & Campana, 2001).

Perceptual learning experiments with stimuli involving lateral masking (Polat & Sagi, 1994b, 1995; Polat, Ma-Naim, Belkin & Sagi, 2004) have suggested that practice is able to modulate short- and long-range lateral interactions between neurons responding to collinear elements. These studies showed that contrast thresholds for a target are modulated by the presence collinear flankers, and the type of modulation depends on the distance between the central target and the flankers: inhibitory for short target-to-flankers distance, and facilitatory for longer distances. With the training the suppression from the short target-flanker separation can be reduced and facilitation at relatively long target-flanker separation increases. These studies suggest that practice on lateral interactions increases the efficacy of the collinear interactions between neighbouring neurons, an effect that enhances connectivity with remote neurons via a cascade of local interactions.

Most importantly, perceptual learning on lateral interactions has been showed to be useful for improving contrast sensitivity in people with normal low vision (Tan & Fong, 2008; Polat, 2009) or with impaired lateral interactions such as amblyopia (Polat et al., 2004). Notably, these studies showed that, differently from previous perceptual learning experiments where non transfer of learning to different stimulus attributes was observed, the effect of training on lateral interactions transferred to higher level visual

tasks, like visual acuity (VA) (Tan & Fong, 2008) producing a long-lasting perceptual benefit in everyday visual tasks.

However, in all these studies stimuli were presented in the fovea. This thesis aimed at investigating the possibility that the effect of training also improves lateral interaction in retinal regions eccentric with respect to the fovea. Lateral interactions strongly depend on eccentricity: in the periphery they are mostly inhibitory (Petrov, Carandini & McKee, 2005; Cavanaugh et al., 2002). These evidence leads to the hypothesis that peripheral vision may acquire some of the functional role of the fovea only if inhibition is reduced. Shani & Sagi (2005) showed that collinear facilitation in the near-periphery is weak and that perceptual learning seems not to be effective in modulating lateral interactions. However, in their study the training was very short, and only one target-to-flanker distance was tested. If lateral interactions could be modulated in the near periphery, and transfer to visual tasks such as VA and crowding was possible, this could be extremely important for rehabilitation of individuals with loss of central vision, such as in macular degeneration. These type of patients, after the loss of central vision, are forced to use the periphery of the visual field for the most demanding visual tasks like face recognition and reading.

In Experiment 1, we were interested in verifying whether inhibitory lateral interactions in the near-periphery (4 degrees of eccentricity) may be reduced by training and if training transfers to other visual functions.

Eight subjects were trained with different spatial frequencies (1, 2, 4, and 8 cycles per degree - cpd) and different target-to-flankers separations (2λ, 3λ, 4λ, and 8λ). Before the practice sessions subjects performed a series of pre-tests aimed at measuring their peripheral contrast sensitivity function (CSF), peripheral visual acuity (VA) and crowding effect. Consistently with previous studies (Petrov et al., 2005; Cavanagh et al., 2002), results of the Experiment 1 showed that, in the near periphery, lateral interactions are inhibitory even at target-to-flanker distances (4λ) where facilitatory interactions are found in central vision. Facilitation was reported for a target-to-flankers distance of 8λ, consistently with the most recent investigation on peripheral lateral interactions (Lev & Polat, 2011). Most importantly, Experiment 1 showed that lateral interactions in parafoveal vision can be modulated by training, reducing the inhibition, and that perceptual learning transfers to other visual abilities, leading to a reduction of crowding.

Since learning specificity is viewed as the main indicator of the level of processing at which learning takes place, and since learning of lateral interaction has been shown to transfer to different visual functions, in Experiment 2 we tested the specificity of learning to basic stimulus features such as target-flankers local and global orientation and retinal position. We trained 4 new subjects in contrast detection of a collinearly flanked vertical target, and found a significant learning effect for the trained configuration but no transfer of learning to either the same stimulus presented in a symmetrical retinal location, nor to a 45 deg oriented collinear target-flankers configuration, presented in the same retinal position as the learning stimulus. The finding that these transfer stimuli are immune to perceptual learning of vertical orientations strongly suggests that the modulation of lateral interactions through perceptual learning is functionally specific, and that transfer to different visual functions can only occur when these are based on the specific early mechanism that is learned.

In Experiment 3, we aimed at exploiting the effects of the perceptual learning of lateral interactions for improving peripheral vision in patients affected by macular degeneration. Training consisted in a contrast detection of a Gabor target with collinear high contrast Gabor flankers, at different target-to-flankers separations, located in their preferential retinal locus (PRL, the new fixation point that spontaneously emeges in this type of patients) and in a symmetrical location.

The rationale behind the measuring or lateral interactions and the training in the PRL and in another retinal location was to point out possible differences in intracortical connectivity for this new fixation point respect to other retinal spots.

Consistently with other studies (Dilks, Baker, Peli and Kanwisher, 2009), we did not find major differences in terms of lateral interactions and perceptual learning effects between PRL and the symmetrical locus.

Training increased contrast sensitivity, and, despite not having any effect on crowding, improved visual acuity in the maculopathy subjects. The absence of crowding reduction could be due to a “roof effect”, since this type of patients naturally train their peripheral view, probably reaching their maximal performance even before the training.. Nevertheless, the improvement of visual acuity opens new perspectives for the rehabilitation of patients with macular degeneration, but also for improving peripheral

vision in normal-sighted subjects, since recent studies showed the important role of the periphery of the visual field in tasks such as postural stability, locomotion and driving.
In Experiment 4, we investigated the architecture of peripheral lateral interactions in a maculopathy patients, finding collinear facilitation at shorter target-to-flankers separation respect to normal-sighted subjects. Interestingly, collinear facilitation was reported for target presentation in the PRL but not in the No-PRL, where collinear interactions were only inhibitory. Moreover, perceptual learning training appeared to be effective in modulating lateral interactions only in the PRL, questioning the hypothesis of a "use-dependent" cortical reorganization, supported, among the others, by Dilks et al. (2009).

Un modo in cui la visione periferica può acquisire il ruolo funzionale della fovea, la parte della retina preferenzialmente utilizzata per compiti visivi complessi (come la lettura e il riconoscimento dei volti) è tramite la modulazione della forza delle connessioni intracorticali presenti nelle aree visive umane tramite apprendimento percettivo. L'apprendimento percettivo è un miglioramento della prestazione n un compito visivo in seguito alla pratica, può mantenersi per diversi mesi ed è specifico per lo stimolo, il computo e l'occhio utilizzato nel training e per il locus retinico in cui è avvenuta la stimolazione. Questi effetti di specificità sono stati spiegati sulla base della plasticità neurale, che consiste in una modifica a lungo termine di alcuni meccanismi presenti nelle prime aree visive corticali, selettive per caratteristiche basilari dello stimolo (Karni & Sagi, 1991, 1993; Ahissar & Hochstein, 1993, 1996; Casco & Campana, 2001).
Esperimenti di apprendimento percettivo con stimoli di mascheramento laterale (Polat & Sagi, 1994b, 1995; Polat, Ma-Naim, Belkin & Sagi, 2004) hanno dimostrato che la pratica può modulare interazioni laterali a breve e lungo raggio tra neuroni che rispondono ad elementi collineari. Questi studi mostrano che le soglie di contrasto per un target centrale sono modulate dalla presenza di elementi vicini, orientati col linearmente, e che il tipo di modulazione dipende dalla distanza tra il target centrale e gli elementi vicini (flankers): inibitoria per brevi distanze tra target e flankers,

facilitatoria per distanze maggiori. Con la pratica, l'inibizione per le brevi distanze target-flankers può essere ridotta e la facilitazione a maggiori distanze aumenta. Questi studi suggeriscono che la pratica sulle interazioni laterale può aumentare l'efficacia delle interazioni collineari tra neuroni vicini, un effetto che aumenta la connettività con neuroni più lontani in seguito ad una cascata di interazioni locali. Inoltre, è stato dimostrato che l'applicazione dell'apprendimento percettivo sulle interazioni laterali produce risultati effettivi nel miglioramento della sensibilità al contrasto in individui con miopia (Tan & Fong, 2008; Polat, 2009) o con interazioni laterali abnormali, come nel caso dell'ambliopia (Polat et al., 2004). Questi studi dimostrano che, a differenza dai precedenti esperimenti sull'apprendimento percettivo che non riportavano il trasferimento del miglioramento ad altri compiti, l'effetto della pratica sulle interazioni laterali si trasferisce ad abilità visive di più alto livello, come l'acuità visiva (Tan & Fong, 2008), dando luogo a benefici percettivi a lungo termine nella quotidianità di questi soggetti. Tuttavia, negli studi finora condotti, gli stimoli venivano presentati in fovea. In questa tesi, l'obiettivo è stato quello di studiare la possibilità che gli effetti del training possano migliorare le interazioni laterali in regioni retiniche periferiche rispetto alla fovea. Le interazioni laterali dipendono fortemente dall'eccentricità: nella periferia del campo visivo sono principalmente inibitorie (Petrov, Carandini & McKee, 2005; Cavanaugh et al., 2002). Questa evidenza porta ad ipotizzare che la visione periferica possa acquisire il ruolo funzionale della fovea solo se l'inibizione viene ridotta.

Shani & Sagi (2005) hanno dimostrato che la facilitazione collineare nella periferia del campo visivo è debole e che l'apprendimento percettivo non sembra efficace nel modulare le interazioni laterali. Tuttavia, nel loro studio il periodo di pratica era molto breve, in più le distanze target-flankers testate erano ridotte. Se le interazioni laterali possono essere modulate nella periferia del campo visivo, e trasferire il miglioramento ad abilità visive come l'acuità visiva o il crowding (affollamento visivo), questo risultato sarebbe estremamente importante per la riabilitazione di individui con perdita della visione centrale, come nel caso della maculopatia.

Questo tipo di pazienti, dopo la perdita della visione centrale, sono obbligati ad usare la periferia del campo visivo per i compiti visivi più complessi, come la lettura ed il riconoscimento dei volti.

Nell'Esperimento 1, l'obiettivo era verificare se le interazioni laterali inibitorie nella periferia del campo visivo (4 gradi di eccentricità) potevano essere ridotte dall'apprendimento e se l'eventualmente miglioramento si trasferiva ad altre funzioni visive. I soggetti sono stati allenati con diverse frequenze spaziali (1, 2, 4, and 8 cicli per grado) e diverse distanze target-flankers (2λ, 3λ, 4λ e 8λ). Prima delle sessioni di pratica, ai soggetti venivano misurate le prestazioni di base in una serie di compiti visivi, come la sensibilità al contrasto periferica (CSF), l'acuità visiva periferica (VA) e l'effetto di crowding (affollamento visivo).Coerentemente con studi precedenti (Petrov et al., 2005; Cavanagh et al., 2002), i risultati dell'Esperimento 1mostrano che, nella periferia del campo visivo, le interazioni laterali sono inibitorie anche a distanze target-flankers che producono facilitazione in visione centrale (4λ). La distanza alla quale è stata trovata la facilitazione in periferia (8λ), è coerente coi più recenti studi sulle interazioni laterali nella periferia del campo visivo (Lev & Polat, 2011). Soprattutto, l'Esperimento 1 mostra che le interazioni laterali in parafovea possono essere modulate dalla pratica, riducendo l'inibizione, e che l'apprendimento percettivo trasferisce il miglioramento ad altre abilità visive, portando alla riduzione del fenomeno di affollamento visivo (crowding). Dato che la specificità dell'apprendimento è considerata l'indicatore principale del livello di processamento dell'informazione in entrata a cui l'apprendimento si verifica, nell'Esperimento 2 abbiamo testato la specificità dell'apprendimento per caratteristiche base dello stimolo come l'orientamento locale e globale degli elementi utilizzati durante il training e la loro posizione spaziale. Un nuovo gruppo di soggetti è stato allenato in un compito di detezione del contrasto per uno stimolo centrale affiancato da elementi collineari, mostrano un effetto di apprendimento significativo per la configurazione allenata, ma non riportando alcun trasferimento per lo stesso stimolo presentato in una posizione retinica simmetrica, né per configurazioni con orientamento locale (tra gli elementi) o globale differente.

L'evidenza che questi stimoli sono immuni all'apprendimento percettivo suggerisce in maniera decisa che la modulazione delle interazioni laterali tramite apprendimento percettivo sia specifica per la funzione, e che il trasferimento a diverse funzioni visive può avere luogo solo quando queste sono basate su specifici meccanismi precoci.

Nell'Esperimento 3, abbiamo testato la possibilità di utilizzare gli effetti dell'apprendimento percettivo delle interazioni laterali per migliorare la vision periferica in pazienti affetti da degenerazione maculare. Il training consisteva in un compito di detezione del contrasto per uno stimolo centrale affiancato da elementi collineari, collocati a diverse distanze target-flankers, presentati nel locus retinico preferenziale (PRL, il nuovo punto di fissazione che spontaneamente questi pazienti sviluppano) ed in una posizione simmetrica. L'idea alla base della misurazione delle interazioni laterali e dell'apprendimento nel PRL ed in un'altra posizione retinica era di verificare se vi siano differenze nella connettività intracorticale tra il nuovo punto di fissazione periferico ed un altro locus retinico. Coerentemente con altri studi ((Dilks, Baker, Peli and Kanwisher, 2009), non abbiamo riscontrato evidenti differenze in termini di interazioni laterali ed effetti di apprendimento percettivo tra PRL e il locus retinico simmetrico.Il training ha migliorato la sensibilità al contrasto e, pur non avendo avuto effetto sul crowding, ha migliorato l'acuità visiva nei soggetti maculopatici. L'assenza di riduzione del crowding può essere dovuta ad un "effetto tetto", dato che questo tipo di pazienti allenano "naturalmente", nella quotidianità, la loro visione periferica, e probabilmente hanno raggiunto la massima prestazione possibile nella visione periferica prima di iniziare il training. Nondimeno, il miglioramento nell'acuità visiva apre nuove prospettive per la riabilitazione di pazienti con maculopatia, ma anche per migliorare la visione periferica in soggetti normovedenti, dato che studi recenti hanno mostrato l'importante ruolo della periferia del campo visivo in attività come la stabilità posturale, la locomozione e la guida.

Nell'Esperimento 4, abbiamo studiato l'architettura delle interazioni laterali periferiche in un soggetto maculopatico, trovando facilitazione collineare a distanze target-flankers minori rispetto ai soggetti normovedenti. Il dato interessante è che la facilitazione collineare emerge solo per la presentazione del target nel PRL, mentre nel PRL le interazioni collineari sono solo inibitorie. Inoltre, l'apprendimento percettivo sembra efficace nel modulare le interazioni laterali solo nel PRL, mettendo in discussione l'ipotesi "uso-dipendente" per la riorganizzazione corticale, supportata, tra gli altri, da Dilks et al. (2009).